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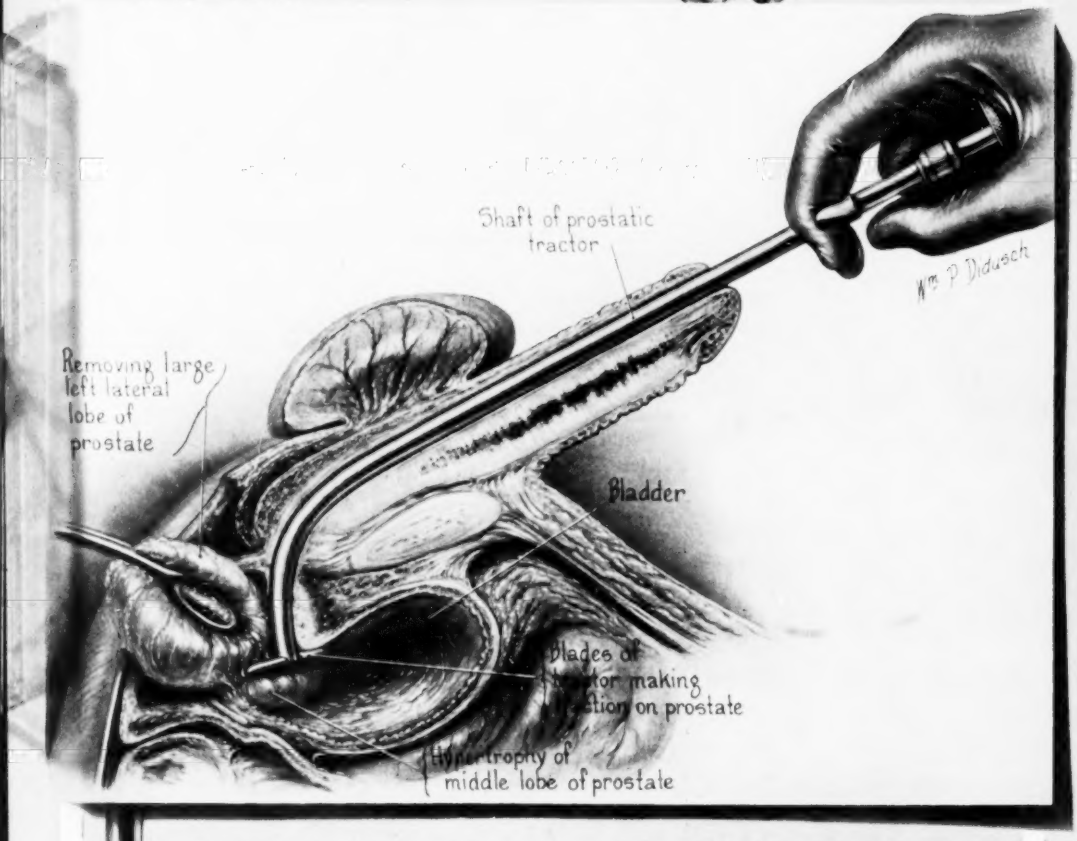
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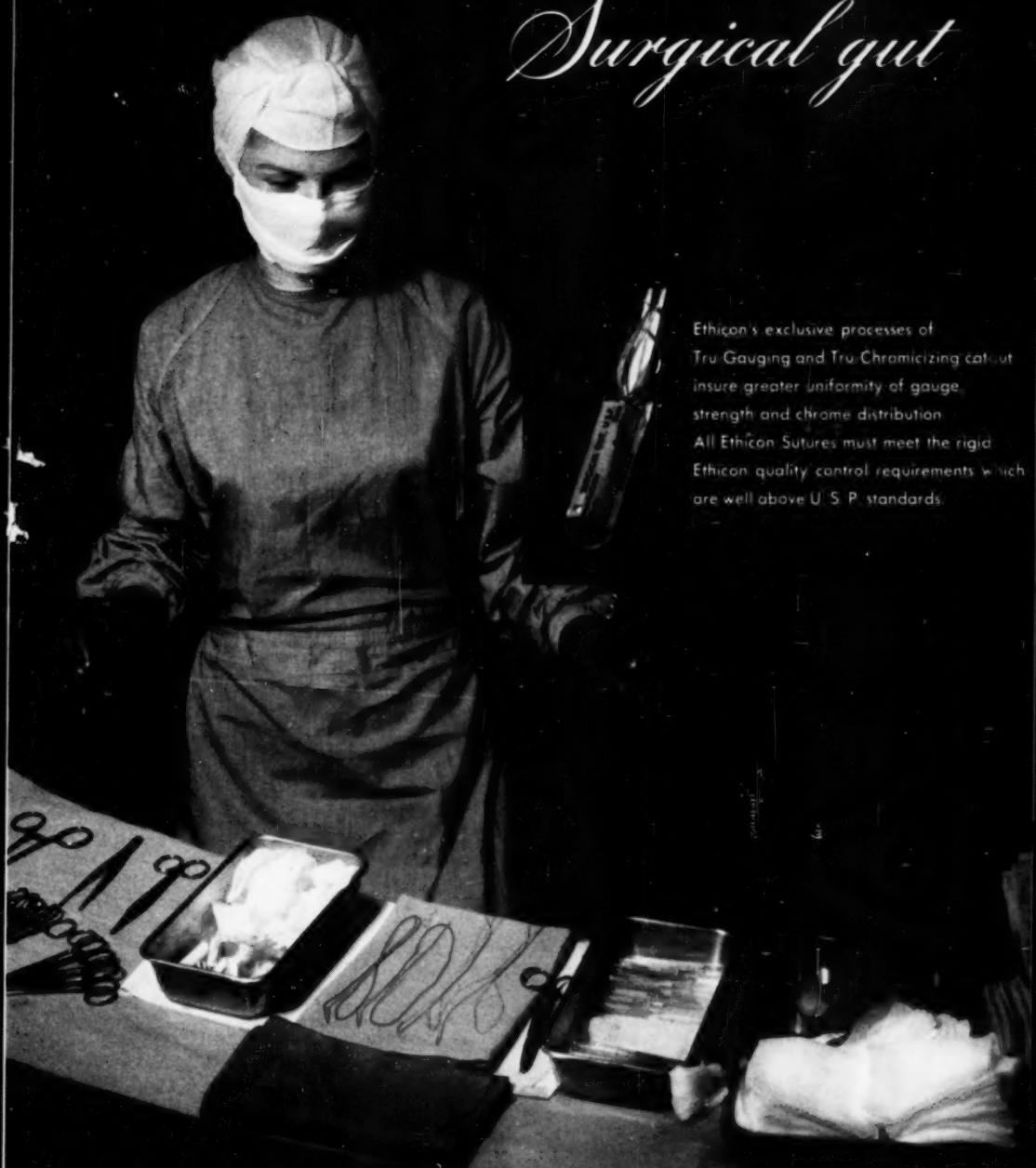

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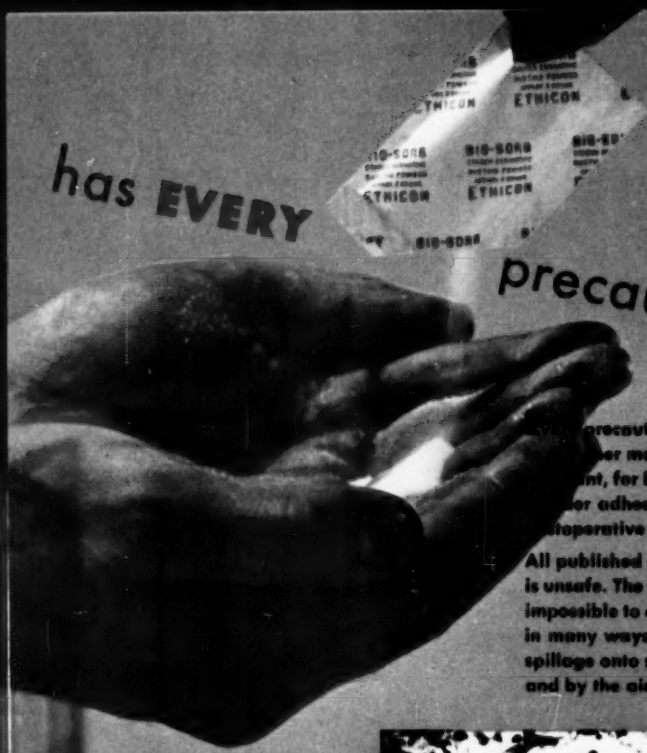

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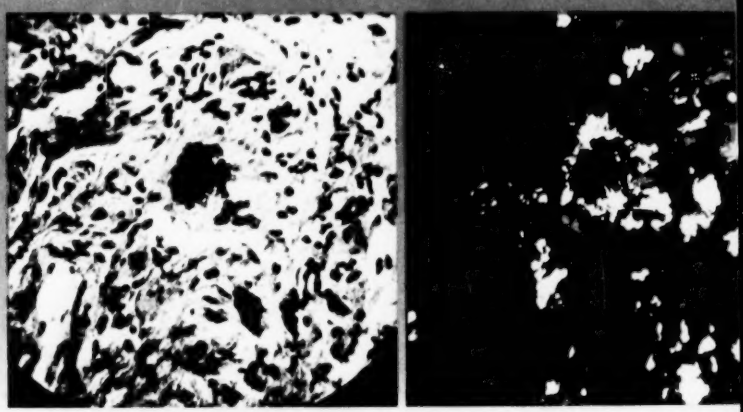

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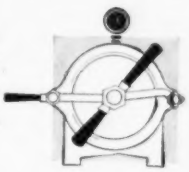

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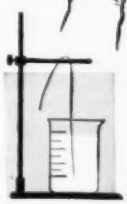

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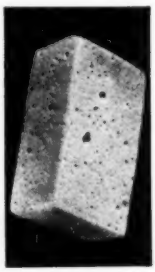
"Plastic Sponge Which Acts As A Framework For Living Tissue," by John H. Grindlay, M.D., and John M. Waugh, M.D., Rochester, Minn. *A.M.A. Archives of Surgery, 63,* 3, Sept. 1951.



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Some experiments were terminated after one month, some between six and eighteen months, and some are still in progress. In almost all cases, the sponge did not become fixed to surrounding tissue, although blood vessels and connective tissue grew into it. Gross and microscopic examinations of the excised sponge and surrounding tissues showed no evidence of inflammatory reactions, with recognizable cellular tissue fitting into spaces not occupied by sponge substance.

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Polyvinyl sponge was employed in 17 plombage operations on 14 patients to fill the space some time after extrapleural pneumothorax, and as a prosthesis following resection. In most cases bacilli rapidly disappeared from the sputum. (A. Hurst, *et al., Diseases of Chest, 20,* 2, Aug. 1951, 134-138.)

● **Abdominal Aneurysms**—Polyvinyl sponge has been successfully used to reinforce large abdominal aneurysms since April, 1950. Four cases to date have been successfully treated by placing sheets of polyvinyl sponge between the aneurysm and peritoneum. Since no other surgical procedure can be used in these cases, and since this operation is simple and without undue strain on the patient, its use appears justified at this stage.

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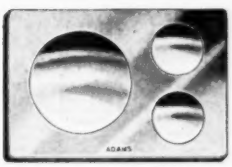
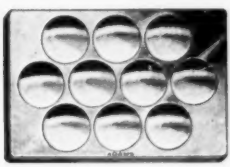
Adaptation of cardiolipin antigen to the Mazzini technic will be found in *Journal of Immunology*, 66, 2, Feb. 1951, 261-275.



For spinal fluid



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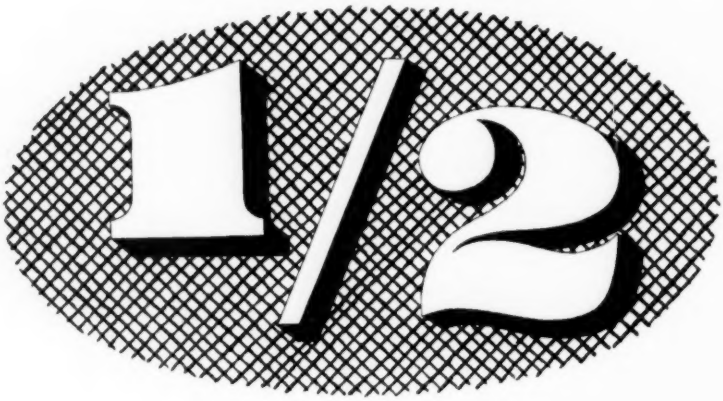

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A. M. A.
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VOLUME 64 FEBRUARY 1952 NUMBER 2

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Editorials

HAS GASTRIC ANALYSIS ANY VALUE?

IN AN EDITORIAL written in 1943 for *Gastroenterology*, Rudolph Schindler [1] suggested that in military hospitals gastric analysis be abandoned as a routine method. In the same issue, Walter C. Alvarez [2] expressed his dissatisfaction with this time-honored test in a somewhat similar vein. He pointed out, "The trouble is that most of the acid values commonly reported by the laboratory are perfectly compatible with a diagnosis of either normal stomach, gastritis, gastric ulcer, duodenal ulcer, gall stone or gastric cancer." Both Schindler and Alvarez had in mind the measurement of the concentration of free hydrochloric acid in a sample of gastric content removed either one hour after the administration of an Ewald meal or of fractional samples of gastric content removed at 10- or 15-minute intervals. It is probable that most internists and surgeons today would agree that gastric analysis by means of the Ewald test meal, the fractional gastric analysis of Rehfuss, or a measurement of the secretory response to the injection of histamine cannot be depended upon to differentiate between a benign and a malignant ulcer in the stomach or to indicate the presence of an ulcer in the duodenum.

Perhaps the greatest deficiency in these methods of gastric analysis depends upon the fact that they are qualitative rather than quantitative in nature. Thus a measurement of the free acid concentration in a sample of gastric content provides little or no information concerning the total amount of gastric juice that is secreted in a given period of time, either in the resting stomach or in response to a specific gastric stimulant. Pavlov believed that the parietal secretion is always produced with a constant concentration of free hydrochloric acid and that variations in the acidity of the gastric content are due to dilution and neutralization by the admixture of food, saliva, mucus from the pyloric antrum, and regurgitated duodenal juices. This view of Pavlov seems to be correct, at least when the electrolyte concentration of the blood is within normal limits. Because of this fact, much more precise information concerning gastric function can be obtained if accurate measurements are made of both the free acid concentration and the volume of secretion poured into the stomach in a measured interval of time. Thus, in the performance of the histamine test the stomach is emptied by aspiration through an indwelling nasal tube, 1 mg. of histamine base is administered by subcutaneous injection, and the gastric content is continuously aspirated for a period of 90 minutes from the time of injection or until the secretory effect of the histamine has subsided. The amount of acid produced by a

From the Department of Surgery of the University of Chicago.

1. Schindler, R.: Gastric Analysis as Routine Military Procedure, Gastroenterology **1**:532, 1943.

2. Alvarez, W. C.: What Value Has Gastric Analysis? Gastroenterology **1**:534, 1943.

standard dose of histamine may be calculated by multiplying the free acid concentration by the volume of content removed, and when this is done, it is usually found that a patient with duodenal ulcer will secrete from two to three times as much acid in response to a standard dose of histamine as is produced by normal persons. The insulin test can be used in a similar manner and the gastric content recovered for a two- or three-hour period following the intravenous injection of 20 units of regular insulin. One of the difficulties encountered with the quantitative collection of gastric secretion after the administration of insulin depends upon the fact that insulin hypoglycemia stimulates not only gastric secretion but also gastric motility, and more of the gastric content escapes into the duodenum than during the control period. For this reason, a curve constructed of the concentration of free hydrochloric acid in fractional 10-minute samples is usually more dependable. Ihre, Winkelstein, and I have each reported that duodenal ulcer patients in general produce more hydrochloric acid in response to insulin hypoglycemia than do normal persons.

It should be kept clearly in mind that tests that determine the capacity of the gastric mucosa to respond to a powerful stimulant are entirely different in their significance from measurements of the gastric secretion in the absence of such stimulation. Much of the newer information on the pathogenesis of peptic ulcer has indicated that this lesion is due to the corrosive, digestant action of the gastric content. The corrosive properties of the gastric content, in turn, are chiefly due to the free hydrochloric acid and pepsin of the gastric juice. Other substances present, such as food, saliva, mucus, and intestinal juices, must be considered as protective or buffering materials. It is clear, then, that the gastric juice secreted in the intervals between meals is more apt to damage the mucous membrane than is the juice secreted in response to the ingestion of food. For these reasons, during the past 10 years we have largely abandoned the traditional methods of gastric analysis in favor of a study of the continuous or fasting secretion of gastric juice in the empty stomach at night. Here the contrast between the patient with duodenal ulcer and the normal person or the patient with gastric ulcer or gastric carcinoma is very striking. This difference is again made evident only when quantitative studies are made. It has been our practice to give the patient to be studied a liquid diet for 24 or 48 hours before the test to insure the absence of solid material in the stomach. An intragastric nasal tube is introduced at 9 o'clock in the evening, with the tip extending to the greater curvature of the stomach as determined by fluoroscopic control. The stomach is emptied and the specimen discarded. Continuous suction is maintained with the Wangensteen apparatus until 9 o'clock the following morning. From time to time during the night the apparatus is checked when feasible to see that it is working and the tube is not plugged with mucus. The volume secured by this aspiration is carefully measured and its free acid concentration determined by titration using Toepfer's reagent. The product of the free acid concentration expressed in clinical units, and the volume expressed in liters, gives the output of free hydrochloric acid in milliequivalents. Normal persons and nonulcer patients tested in this manner were found to secrete quite regularly an average of 18 mEq. of free hydrochloric acid in a 12-hour period at night when the alimentary tract is empty of food, and the patient shielded from the sight, odor, or taste of food. Patients with gastric ulcer or carcinoma of the stomach put out the same or smaller quantities of hydrochloric acid. On the other hand, patients with duodenal ulcer secrete an average of 60 mEq., or

more than three times the normal value. In a series of 600 ulcer patients in whom this test was made, 60 put out over 100 mEq. of hydrochloric acid and two of them the astounding total of 350 mEq. Patients complaining of night pain were invariably found to be hypersecreters. This test proved to be of great value in selecting patients for treatment by gastric vagotomy and in advising patients concerning the possibilities of medical treatment. Thus it is highly unlikely that the two patients who put out over 300 mEq. of hydrochloric acid in their night secretion could be treated by any type of neutralization therapy that would be endurable for any long period. The fact that this night secretion persists even in ulcer patients sound asleep under the influence of narcotic drugs indicates a limitation in this type of sedative therapy.

Not only is a quantitative estimation of the output of hydrochloric acid in the fasting stomach of value in prognosis and in the selection of medical or surgical treatment for duodenal ulcer, but it is likewise of great value in the postoperative follow-up of patients. The profound reduction in the output of free hydrochloric acid following an adequate gastric vagotomy is a more dependable criterion of the probable success of the operation than is the response to insulin hypoglycemia. Thus in our experience we have seen patients in whom the hypersecretion of gastric juice in the fasting stomach has been reduced to secretion below the normal level even though a few vagus fibers have remained intact, as indicated by a positive response to insulin hypoglycemia. Postoperative estimations of the fasting secretion should be made immediately after surgery, whether this be vagotomy and gastroenterostomy or partial gastric resection, and repeated again at the end of three months, at the end of a year, and then at yearly intervals. If the output of free hydrochloric acid in the fasting secretion persists below the level found in normal people, the prospect of permanent relief in the case of duodenal or gastrojejunal ulcer is excellent. No longer need it be said, once an ulcer patient, always an ulcer patient.

LESTER R. DRAGSTEDT, M.D.

MEDIASTINAL GASTRIC CYST

Successful Excision in an Eight-Week-Old Infant

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AMONG the heterogeneous group of developmental anomalies known as enteric duplications, mediastinal gastric cysts are of outstanding surgical importance, because without operative treatment they are almost invariably fatal. In the general category of mediastinal tumors, gastric cysts are extremely rare. Unlike other mediastinal cysts they are almost never asymptomatic. For this reason they are discovered in disproportionate numbers in the first decade of life and are actually one of the commonest mediastinal cysts encountered in infancy. Until recently, comparatively few examples of successful excision of these cysts have been reported, most of the cases being discovered at autopsy. Within the last five years the number of cases reported has almost doubled and practically all the recent articles record successful operations.

We have been able to find 32 examples of intrathoracic gastric cysts [1] in the literature. In the report that follows an additional case will be described. This infant was operated on when 8 weeks old and has now been followed for a four-year period. This patient and the one recently operated on by Leahy and Butsch [17] are the youngest yet to be reported in whom complete extirpation was done.

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1. (*a*) Staehelin-Burckhardt, A.: Über eine mit Magenschleimhaut versehene Cyste des Oesophagus, Arch. Verdgskrkh. **15**:584, 1909. (*b*) Mixter, C. G., and Clifford, S. H.: Congenital Mediastinal Cysts of Gastrogenic and Bronchogenic Origin, Ann. Surg. **90**:714, 1929. (*c*) Smith, R. E.: A Case of Mediastinal Dermoid Cyst in an Infant, Guy's Hosp. Rep. **80**:466, 1930. (*d*) Fischer, W.: Über eine Cysts in der rechten Pleurahöhle, Arch. path. Anat. **275**:711, 1930. (*e*) Entz, B., and Orosz, D.: Über die intrathorakalen Zystenbildungen, Frankfürt. Ztschr. Path. **40**:229, 1930. (*f*) Poncher, H. G., and Milles, G.: Cysts and Diverticula of Intestinal Origin, Am. J. Dis. Child. **45**:1064 (May) 1933. (*g*) Böss, C.: Kongenitale, mit Magenschleimhaut ausgekleidete Mediastinalcyste mit in die Lunge penetrierendem chronischem Ulcus pepticum, Arch. path. Anat. **300**:166, 1937. (*h*) Seydl, G. N.: Eine kongenitale Magenwandcyste im Mediastinalraum mit in die Lunge perforiertem Ulcus pepticum, Frankfurt. Ztschr. Path. **52**:346, 1938. (*i*) Nicholls, M. F.: Intrathoracic Cyst of Intestinal Structure, Brit. J. Surg. **28**:137, 1940. (*j*) Carlson, H. A.: Congenital Cysts of the Mediastinum, J. Thoracic Surg. **12**:376, 1943. (*k*) Olken, H. G.: Congenital Gastro-Enteric Cysts of the Mediastinum, Am. J. Path. **20**:997, 1944. (*l*) Schwarz, H., II, and Williams, C. S.: Thoracic Gastric Cysts, J. Thoracic Surg. **12**:117, 1942. (*m*) Ward, I. M., and Krahl, J. B.: Enterogenous Pulmonary Cyst, Am. J. Dis. Child. **63**:924, 1942. (*n*) Wyllie, W. G., and Pilcher, R. S.: Intrathoracic Cysts of Intestinal

REPORT OF A CASE

The patient was a full-term, male infant whose birth weight was 7 lb. 3 oz. (3.3 kg.); delivery was spontaneous. At birth he appeared normal except that the respiratory rate was rapid. When feedings were started, he appeared to have difficulty in swallowing, frequently regurgitated the formula, and at such times often became alarmingly pale. The symptoms persisted, particularly the alarming pallor which followed regurgitation of the formula. At 6 weeks of age a roentgenogram of the chest was made [2] and a large tumor in the right hemithorax was demonstrated.

When first seen by one of us on March 11, 1946, the infant was 7 weeks old; his weight was 8 lb. 15 oz. (4 kg.). At this time the respiratory rate was somewhat accelerated, and he was slightly pallid. Physical examination demonstrated no additional findings except some impairment of the percussion note and diminished breath sounds over the right lower lobe.

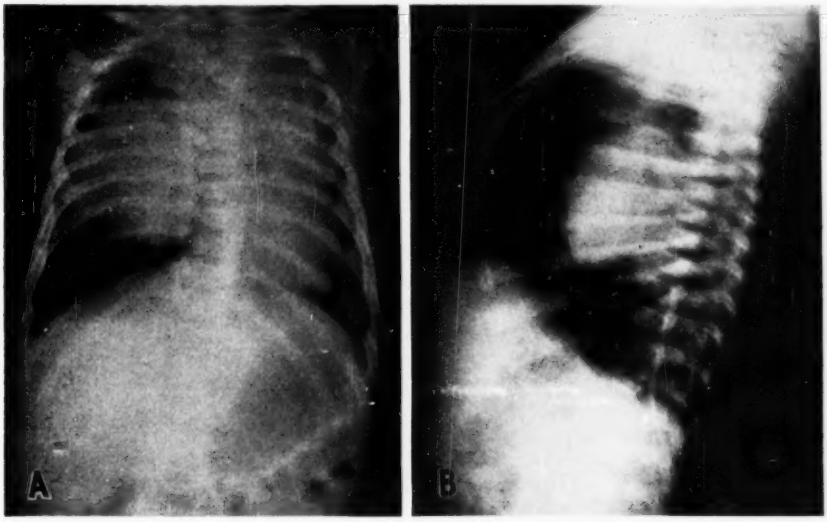

Fig. 1.—*A*, anteroposterior roentgenogram in the supine position demonstrates the cyst in the right hemithorax. The mediastinum is widely displaced to the left. *B*, right lateral roentgenogram demonstrates the posterior position of the cyst. This view and the study reproduced in *A* illustrate the typical roentgen appearance of this anomaly.

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and Bronchial Structure, Arch. Dis. Childhood **18**:34, 1943. (*o*) Ladd, W. E., and Scott, H. W., Jr.: Esophageal Duplications or Mediastinal Cysts of Enteric Origin, Surgery **16**:815, 1944. (*p*) Steele, J. D., and Schmitz, J.: Mediastinal Cyst of Gastric Origin, J. Thoracic Surg. **14**: 403, 1945. (*q*) Laipply, T. C.: Cysts and Cystic Tumors of the Mediastinum, Arch. Path. **39**:153, (March) 1945. (*r*) Dickson, J. A.; Clagett, O. T., and McDonald, J. R.: Intrathoracic Gastric Cyst, J. Thoracic Surg. **15**:318, 1946. (*s*) Valle, A. R., and White, M. L., Jr.: Thoracic Gastric Cyst, Ann. Surg. **123**:377, 1946. (*t*) Jones, J. C.: Esophageal Duplications or Mediastinal Cysts of Enteric Origin, West. J. Surg. **55**:610, 1947. (*u*) Davis, E. W., and Salkin, D.: Intrathoracic Gastric Cysts, J. A. M. A. **135**:218, (Sept. 27) 1947. (*v*) Davidson, L. R., and Brown, L.: Gastrogenous Mediastinal Cyst, J. Thoracic Surg. **16**:458, 1947. (*w*) Ehler, A. A., and Atwell, S.: Gastric Cyst of the Mediastinum, ibid. **17**:809, 1948. (*x*) Curreri, A. R., and Gale, J. W.: Mediastinal Tumors, Arch. Surg. **58**:797, (June) 1949. (*y*) Leahy, L. J., and Butsch, W. L.: Surgical Management of Respiratory Emergencies During the First Weeks of Life, ibid. **59**:466, (Sept.) 1949.

2. Dr. M. Edward Miller, Roscoe, N. Y.

The patient was hospitalized at once, and additional roentgenograms of the chest were made (Fig. 1). Data referable to examination of the blood and urine were not remarkable. A pediatric consultation [3] was obtained, and a decision to proceed with operation was made. Our preoperative diagnosis was mediastinal tumor; because of its size and location, mediastinal gastric cyst was considered. Preliminary to operation a cannula was introduced into the left internal saphenous vein at the ankle, and an infusion of isotonic sodium chloride was started. The anesthetic agent used was cyclopropane, with a tight-fitting face mask.[4] During the procedure, which required three hours 50 cc. of isotonic sodium chloride and 200 cc. of blood were administered.

Operation (April 18, 1946).—A long curvilinear incision was made over the sixth rib, and a small segment of the posterior end of it was removed. The pleural space was entered

Fig. 2.—Photograph of the gross specimen after repair of the opening made at operation and distention with water. The cyst is actually somewhat smaller as compared with its size at operation.

through the sixth interspace, and a self-retaining retractor was introduced. When the latter was opened widely the seventh rib was fractured at its angle. The infant's color was slightly dusky up to the time the pleura was opened. At this time it improved remarkably and was excellent during the remainder of the operation.

The exposure was good, and a large, firm grayish-white, tense, cystic mass presented in the posterior mediastinum. It was retropleural in position, and excision was begun by widely opening the pleura at the posterior border of the mass. Between the pleura and the cyst a plane of cleavage was easily found, and enucleation proceeded readily until the region of the inferior pulmonary vein and the esophagus was reached. Here there was considerable edema,

3. With Dr. J. B. Burns.

4. Administered by Dr. C. H. M. Goodman.

which obscured identification of the mediastinal structures. For this reason the cyst was aspirated, and about 100 cc. of murky-white watery fluid was removed.[5] This removal improved the exposure, and dissection proceeded to the level of the esophagus. The cyst was densely adherent here and could not be identified because of edema. The cyst was accordingly opened wide and its contents completely evacuated. There was no communication with the esophageal lumen. The lining of the cyst was covered with mucin, and its appearance was identical to gastric mucosa. The index finger was then introduced into the sac, and this maneuver considerably facilitated the dissection. Finally there remained an area about 2 cm. in diameter where the muscular wall of the cyst was intimately fused with the esophagus. To avoid the

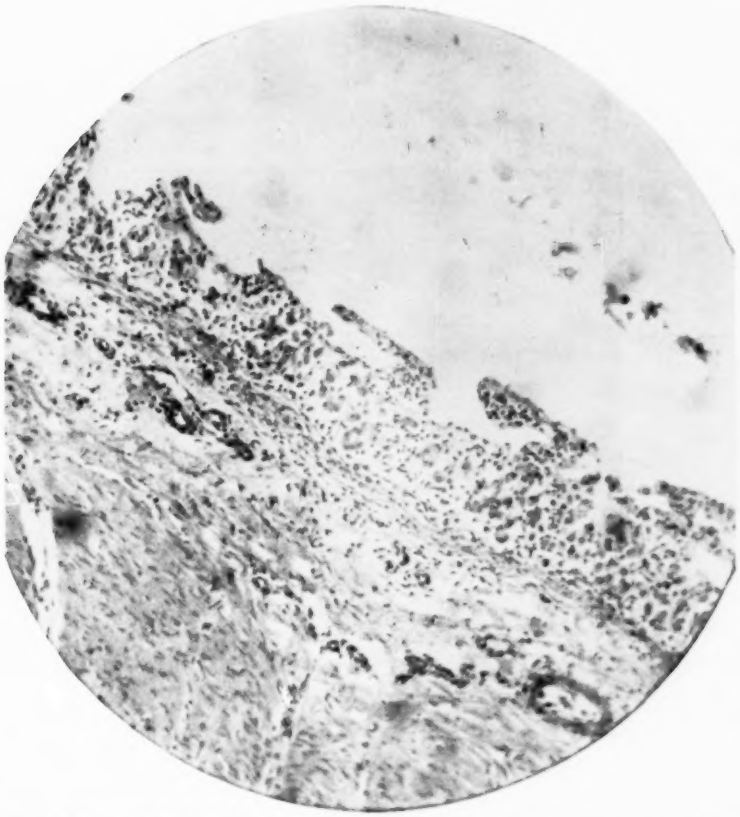

Fig. 3.—The well-developed gastric mucosa lining of the cyst is seen in this high-power photomicrograph.

danger of opening the esophagus, the muscle layer of the cyst at the periphery of this adherent area was divided, the final dissection being an enucleation in the submucosal layer.

The pleural space was flushed out with an excess of saline solution, 10,000 units of penicillin was instilled, and the lung was inflated. The wound was closed in layers without drainage, two No. 32 Babcock wire sutures being used to approximate the ribs and interrupted fine

5. Analysis of the fluid demonstrated 2.80 units of free hydrochloric acid and 14.20 units of combined acidity.

silk for muscles, fascia, and skin. At completion of the operation the infant's condition was good; breath sounds of normal intensity were present over the right lung.

Pathological Report.[6]—Gross Description: The specimen is a firm-walled cyst which measures 5 cm. in diameter and 3 mm. in thickness. The outer surface is shaggy with areolar connective tissue rich in blood vessels; the lining shows low ridges covered with velvety smooth epithelium (Fig. 2).

Microscopic Examination (Benign Gastric Cyst): The mucosa throughout is suggestive of the late fetal stage of development, ranging from single acini, appearing as islands in plentiful stroma, to clusters of acini underlying villous projections in a thicker mucosa. In the better-developed portions acini are lined with fairly large polygonal cells with large central nuclei and pink cytoplasm; these are gastric parietal cells. One submucosal lymph node and a few scattered lymphocytes are seen. The surface lining, including that of the villous projections, is an indistinct, low cuboidal, fetal type of covering.

The circular and longitudinal muscularis are well developed. A distinct muscularis mucosa is very thin in some places and well developed in others. The nerve plexuses of Meissner and

Fig. 4.—Roentgenogram of the chest four years and six months after operation. The defect incident to the thoracotomy is demonstrated; it is otherwise not remarkable.

Auerbach are well developed, and, in addition, nerve bundles and ganglion cells are present in the areolar tissue external to the longitudinal muscle (Fig. 3).

Postoperative Course.—The postoperative course was without incident. The infant was returned to the ward and placed in an oxygen tent. An additional 250 cc. of 5% dextrose in water was administered intravenously during the immediate postoperative period. The morning after operation the infant greedily took his entire formula; subsequent feedings were all taken without any difficulty. Postoperative roentgenograms demonstrated complete expansion of the right lung; no pleural effusion developed. The wound healed by primary union, the stitches were removed on the fifth day, and the infant was discharged from the hospital on the ninth postoperative day.

Subsequent Course.—Since his discharge from the hospital the patient has been well and has developed normally. A bilateral congenital inguinal hernia was first noticed when the child was 3 years old. A recent roentgenogram of the chest is reproduced in Figure 4. This boy is now somewhat better developed than the average 4-year-old child.

6. By Dr. Victor W. Bergstrom, Pathologist, Kilmer Laboratory, Binghamton City Hospital.

INCIDENCE

Congenital mediastinal cysts and tumors of any type are uncommon. In a review of the literature prior to 1945, Laipply [19] discovered 299 mediastinal cysts and tumors of congenital origin. Among these, approximately 80% were dermoids and teratomas, 12% bronchogenic cysts, 5% gastric cysts, and 1.5% enteric cysts. Laipply recorded 31 dermoids and teratomas discovered in patients under 12 years of age and 13 bronchogenic cysts in patients under 10 years; 14 patients with gastric cysts were 10 years of age or younger. Thus, gastric cysts, comprising only 5% of the total series, constituted one-fourth of the lesions discovered in infants and children. Blades [7] in 1946, reviewing 109 mediastinal tumors and cysts which were removed in Army Hospitals, did not report a single instance of gastric cyst. Among 36 examples of mediastinal tumors and cysts recorded by Curreri and Gale,[18] there was only one gastric cyst (occurring in an infant).

These series all emphasize the propensity of cysts of this type to produce symptoms early. Among the 32 patients with intrathoracic gastric cysts that we have studied, one-half were 1 year or younger, 70% were 2 years or younger, and 90% were 6 years or younger; the oldest patient was 23 years of age. There is a slight predominance of males in the series.

EMBRYOLOGY

The nature of the nidus of foregut epithelium which gives rise to mediastinal enteric cysts is unknown. The following explanations are frequently advanced:

1. Mediastinal enteric cysts represent persistent embryonal diverticula.[1f]

2. Enteric duplications represent a failure of coalescence of vacuoles in a transverse direction, with formation of two separate lumina.[8]

3. In the course of evagination of the lung buds a few cells are pinched off which eventually form a cyst.[9] In relevant literature the view is sometimes expressed that all these mechanisms may be involved.[10]

The majority of gastric cysts are located in the region of the middle third of the esophagus, originate in the posterior mediastinum, and extend into the right hemithorax. Their position is so uniform that Olenik and Tandatnick [9a] observed that a needle introduced posteriorly below and just lateral to the transverse process of the fourth thoracic vertebra on the side of the cyst would have pierced all mediastinal cysts of foregut origin then reported. Of the 31 reported instances of gastric cyst in which the side is mentioned, the cyst extended into the right hemithorax in 26. This location could be explained by the extrusion early in foregut differentiation of a nidus of pleuripotential cells from the developing foregut in the region of the lung buds. Schwarz and Williams [11] have proposed the attractive theory that "organizer substances" may play an important role in the development of these anomalies.

7. Blades, B.: Mediastinal Tumors, Ann. Surg. **123**:749, 1946.

8. (*a*) Bremer, J. L.: Diverticula and Duplications of the Intestinal Tract, Arch. Path. **38**:132 (Sept.) 1944. (*b*) Evans, A.: Developmental Enterogenous Cysts and Diverticula, Brit. J. Surg. **17**:34, 1929.

9. (*a*) Olenik, J. L., and Tandatnick, J. W.: Congenital Mediastinal Cysts of Foregut Origin, Am. J. Dis. Child. **71**:466 (May) 1946. (*b*) Schwarz and Williams.[11]

10. Black, R. A., and Benjamin, E. L.: Enterogenous Abnormalities: Cysts and Diverticula, Am. J. Dis. Child. **51**:1126 (May) 1936. Bremer.[8a]

They suggest that an evagination originally under the influence of a lung organizer substance may subsequently be stimulated by stomach organizers to form a replica of the stomach. Those cell rests still retaining a connection with the esophageal wall at the time of the rotation of the stomach would rotate with the ventral esophageal surface to the right. The successive influence of several organizer substances is suggested by these authors as an explanation for the occurrence of cysts which possess a variety of epithelial elements.

The cyst may have no connection with surrounding structures, but its wall often shows varying degrees of fusion with the adjacent esophagus, even to the extent of sharing a common muscular layer, as was present in our case. In no reported instance has intraluminal connection between the gastric cyst and the esophagus been shown. Communication with bronchi may develop through erosion secondary to peptic ulceration.[11]

The mediastinal gastric cyst reported by Poncher and Milles [1f] was associated with an abdominal enterogenous cyst. Spina bifida has been present in several instances.[12] Other accompanying congenital anomalies are not predictably frequent. Arnold-Chiari malformation with cerebellocele and hydrocephalus,[1k] hemivertebrae,[1w] diverticulum of the urinary bladder,[1a] uvula bifida [1a] and accessory spleen [1d] have been reported in isolated instances.

HISTOLOGY

Cysts developing from the primitive foregut may have characteristics of bronchial or enteric tissue. Admixtures frequently occur, making exact classification difficult. In general, cysts having ciliated epithelium and cartilage in their walls are designated bronchogenic; those with epithelium resembling that at varying levels in the alimentary canal with fibrous and muscular walls are termed enteric cysts. Within the general group of enteric cysts, those having epithelium resembling gastric mucosa somewhere within their mucosal linings are designated gastric cysts.

Bronchial and gastric epithelium may coexist.[1a, c] In such instances the question of whether the cyst should be classified as bronchial with gastric mucosa or gastric with bronchial mucosa seems to depend on the predominant characteristics of the mucosal lining and the cyst wall. More frequently, gastric mucosa occurs in conjunction with other enteric mucosal types.[13]

Mediastinal gastric cyst is not regarded as a separate embryological entity. All cysts of foregut origin may, if the mucosa is actively secretory, enlarge and produce similar symptoms. Cysts containing gastric mucosa are singled out for attention because of their frequency within the group, the pressure symptoms which usually appear in the early years, and the peptic ulceration which not infrequently occurs.

SYMPTOMS

Whereas other congenital mediastinal cysts are occasionally encountered in patients of advanced age as an incidental autopsy finding, there has not yet been reported a single instance in which a mediastinal gastric cyst has been discovered in this way. As previously noted, these cysts are rarely asymptomatic, and for the

11. Bõss.[1g] Seydl.[1h] Ward and Krahl.[1m] Valle and White.[1s]

12. Staehelin-Burckhardt.[1a] Olken.[1k] Ehler and Atwell.[1w]

13. Carlson.[1j] Olken.[1k] Schwarz and Williams.[1l] Ward and Krahl.[1m] Laipply.[1q] Jones.[1t]

most part they produce severe symptoms early. Because many are actively secretory, progressive enlargement is the rule and most of the symptoms are due to the enlarging posterior mediastinal mass. As might be anticipated, cough and dyspnea are outstanding features, having been present in more than half of the reported cases. Cyanosis, atelectasis, and pneumonia have also been frequently reported. Symptoms less commonly encountered are vomiting and dysphagia,[14] abdominal pain,[1f, o] and pain in the chest.[11, u] Clubbing of the fingers and toes has been noted in three articles.[15]

In addition to dysphagia, pressure on the esophagus may interfere with its blood supply and produce necrosis of the mucous membrane and hematemesis; hemoptysis due to peptic ulceration into a bronchus also occurs. This type of bleeding has been reported [16] with surprising frequency, and in addition two patients [1f, o] have had blood in their stools. In the patients of Böss [1g] and Seydl [1h] a peptic ulcer eroded into the lung, causing a fatal pulmonary hemorrhage.

In connection with the above, it should be noted that various degrees of acidity of the contents of these cysts have been recorded.[11] The mucosae of the "active" cysts is doubtless stimulated in utero by the maternal blood-borne gastric secretory excitant, and this may explain why these particular cysts by comparison may be so large at birth. Subsequently the infant's own gastric hormone presumably continues to stimulate the gastric mucosa, and this stimulation may be the most important single factor in the progressive enlargement and early fatal outcome that commonly occurs without operation.[17]

ROENTGEN EXAMINATION

As noted in the foregoing paragraphs, gastric cysts produce a confusing variety of symptoms, none of which are particularly characteristic of the anomaly. The x-ray examination, on the contrary, is extremely helpful and when considered together with the symptoms and age of the patient may strongly suggest the diagnosis. The roentgenogram characteristically demonstrates a mass originating in the posterior mediastinum. Among the 32 patients considered in this report, the cyst was present on the right side in 26 and on the left side in five, and in one patient the side was not recorded. The cyst is commonly rather large and of homogenous density; occasionally secondary emphysema,[1s, y] atelectasis,[1f, y] or pneumonitis [13] may obscure the picture. The cyst itself is often originally mistaken for pneumonia so that the actual incidence of pneumonia or atelectasis is difficult to evaluate. Massive pneumothorax has been reported.[1m] The cyst when small is usually spherical but may enlarge in all directions, its outline being determined by the surrounding structures.

14. Mixter and Clifford.[1b] Ladd and Scott.[1o] Ehler and Atwell.[1w]

15. Mixter and Clifford.[1b] Ladd and Scott.[1o] Valle and White.[1s]

16. Fischer.[1d] Poncher and Milles.[1f] Böss.[1g] Seydl.[1h] Ward and Krahl.[1m] Ladd and Scott.[1o] Valle and White.[1s] Ehler and Atwell.[1w]

17. The relationship between the secretion of the stomach and the mucosa of the gastric cyst remains speculative. In Graham's patient, reported on by Lowry and Moorman (Lowry, T., and Moorman, L. J.: Accessory Stomach in the Right Thorax, Am. Rev. Tuberc. **38**:27, 1938), stimulation of secretion in the thoracic gastric cyst was not observed when the infant was fed. Secretion from the cyst appeared to occur independently of the normal gastric secretion at about 12-hour intervals.

The cysts reported by Dickson and others [1f] and by Valle and White [18] were found to have extended through the diaphragm; these cysts were associated with bronchiectasis. Erosion of adjacent ribs,[18] changes in contour of the spine,[19] and asymmetry of the chest [12, 9] are not uncommon. Roentgenograms of the patient reported on by Steele and Schmitz [1p] demonstrated calcification of the superior border of the cyst; such calcification is rare.

Gross and others [20] have recently reported on three patients less than 4 years old having thoracic diverticula arising from the upper small intestine; in each instance the diverticulum passed through the right crus of the diaphragm. In two of these the roentgen examinations demonstrated air in the diverticula, a finding rarely seen in intrathoracic gastric cyst; two of these diverticula contained gastric mucosa.

DIAGNOSIS

Gastric cyst should be suspected, especially in an infant or child, when the chest roentgenogram demonstrates a rounded mass in the posterior mediastinum. These cysts cannot readily be differentiated from neurogenic tumors (notably ganglioneuromas), but their size and the early appearance of pressure symptoms will often aid in this distinction. Their posterior location, smooth contour, and uniform roentgen density help to differentiate gastric cysts from dermoids and teratomas, pericardial celomic cysts, bronchogenic cysts, and thymomas. Mediastinal bronchogenic cysts may occur at any level but are most frequent in the mid-mediastinum; they are frequently attached to the trachea and move with swallowing.[7] For the most part, diagnostic procedures other than conventional roentgenograms are not particularly helpful in establishing a diagnosis of mediastinal gastric cyst. Displacement or narrowing of the tracheobronchial tree may be demonstrated by bronchoscopy or iodized oil studies, but in an already dyspneic patient either procedure may be dangerous. Esophagograms have a limited usefulness and may help to outline the cyst. Aspiration may be employed diagnostically, the fluid being analyzed for titratable acidity, pepsin, rennin, and blood; the finding of hydrochloric acid in the fluid establishes the diagnosis. This procedure may produce pneumothorax or lead to leakage of corrosive cyst contents through the puncture site.[1w]

It is our impression that, for the most part, refined diagnostic studies are unnecessary or dangerous. In every instance the clinical findings and roentgen study will establish a diagnosis of mediastinal tumor, and this is a sufficient indication for thoracotomy.

TREATMENT

Among the 32 examples of intrathoracic gastric cyst which we have found, eight were discovered at autopsy. Twenty-four patients were operated on, and eight died; among those who recovered, the cyst was excised in 12 and marsupialized in 2, and marsupialization and subsequent excision were done in the remaining 2. Results have improved remarkably in recent years. Prior to 1940 there were five operations with four deaths. Ten operations were performed between 1940 and 1944; seven of the patients recovered. Since 1944 nine operations have been

18. Mixter and Clifford.[1b] Poncher and Milles.[1f] Ladd and Scott.[1o] Davis and Salkin.[1u]

19. Fischer.[1d] Entz and Orosz.[1e] Seydl.[1h] Nicholls.[1i] Davis and Salkin.[1u]

20. Gross, R. E.; Neuhauser, E. B. D., and Longino, L. A.: Thoracic Diverticula Which Originate from the Intestine, Ann. Surg. **131**:363, 1950.

reported, and eight of the patients recovered. In two of the patients in this group pulmonary resection was required. The single fatality [18] occurred in a 22-month-old infant in whom peptic ulceration had produced a bronchial fistula, bronchiectasis, and repeated severe pulmonary hemorrhages. A pneumonectomy was required, and cardiac arrest occurred on the operating table. A second patient [17] in this group had associated bronchiectasis and required lobectomy. In both of these patients the cyst extended below the diaphragm.

Ladd and Gross [21] have emphasized the fact that an intimate connection may exist between the muscular layers of the cyst and the esophagus without a line of demarcation; this finding was present in our patient. In such circumstances they have suggested that excision may be contraindicated because of the possibility of interfering with the blood supply to the esophagus. This danger was avoided in our patient by the performance of an enucleation in the submucosal plane of the cyst as previously described. Marsupialization has not been utilized in cases recently published, and in every patient reported on since 1945 excision has been done.

SUMMARY

Successful excision of a mediastinal gastric cyst in an 8-week-old infant is reported. Thirty-two additional cases previously published have been studied, and the embryological and clinical features are discussed. It is emphasized that these rare cysts are seen in disproportionate numbers in infancy and that they may present an urgent indication for operation.

21. Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract, Surg., Gynec. & Obst. **70**:295, 1940.

USE OF PRESERVED TISSUES IN ORTHOPEDIC SURGERY

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NAVAL medicine is once again faced with an influx of war-wounded. Extensive traumatic and reconstructive surgery has been necessary for the proper treatment of many of these wounded. The specific problems of bone replacement and skin coverage of the large wounds suggested that stored bone and skin would be useful in selected cases.

A tissue bank was therefore established as a research project at the Naval Medical School for the purpose of developing methods of tissue procurement, processing and storage. The facilities of the Naval Medical Research Institute for the study of animals were used for experimental surgical evaluation, while the pertinent service of the Naval Hospital, Bethesda, Md., was utilized for investigation of patients. This paper is a report on the status of the research project to date.

In the past six years frozen bone grafts have been proved to be of value by various investigators. Wilson [1] has reported 85% successes in 205 cases. LeCocq [2] had 85.7% successes in 56 operations. Therefore, the initial phase of the tissue bank consisted of the establishment of a deep freeze bone bank, following the principles of Bush and Garber.[3]

In military orthopedic service, certain limitations of frozen bone became apparent. It was noted that the handling and shipping of refrigerated bone is difficult and expensive. Further, frozen bone may have a limited storage time. Speed and Smith [4] noted gross changes in bone stored for periods as short as three months. Wilson has noted several unsatisfactory results with bone stored over a period of one year.

To overcome these limitations, a better method of preservation was sought. For many years plasma, enzymes, bacteria, and biologicals have been successfully preserved by the process of drying from the frozen state. Freeze-dried products can be stored in containers at room temperatures and can be easily shipped. A well-

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1. Wilson: Personal communication to the author.

2. LeCocq, J. F.; LeCocq, E. A., and Anderson, K. J.: Preliminary Report on Use of Bone Bank Bone, Surg., Gynec. & Obst. **91**:277-280, 1950.

3. Bush, L. F., and Garber, C. Z.: Bone Bank, J. A. M. A. **137**:588-594 (June 12) 1948.

4. Speed, J. S., and Smith, H.: Personal communication to the author.

known example is freeze-dried or "lyophilized" plasma, which is chemically, antigenically, immunologically, and electrophoretically stable for five to seven years.[5]

In view of these advantages, it was decided to adapt this technique of preservation to bone. The method is one of freezing the bone at about —40 C. and then drying from the frozen state under a high vacuum. The freeze-dried graft is then hermetically sealed for storage and distribution.

An experimental evaluation of this method of preservation was reported at the American Academy of Orthopedic Surgeons in January, 1951.[6] This experiment was designed to evaluate the response of the dog radius to stored cortical inlay bone grafts. Freeze-dried homogenous grafts were compared with controls of fresh autogenous and frozen homogenous grafts. A defect the size of the graft served as an additional control. Forty animals were killed at intervals of 8 to 260 days. The results indicated that frozen homogenous and freeze-dried homogenous grafts heal in a manner similar to fresh autogenous grafts but at slightly slower rate. In some respects the freeze-dried bone grafts appeared to be superior to the frozen ones.

On the basis of this animal experimentation, a clinical evaluation of freeze-dried bone was initiated. Early clinical results are promising. Final evaluation of the current series will be reported later.

In our frozen bone, 16.3% of the deposits have been rejected because of bacterial contamination. The feasibility of cathode-ray sterilization of bone grafts is being evaluated in conjunction with Dr. John Trump and Mr. Ken Wright, of the High Voltage Research Laboratory at the Massachusetts Institute of Technology. If it is successful, the rigid asepsis necessary for bone processing will be modified.

In 1881 Dr. E. P. Brewer,[7] after completing an autopsy on a tuberculous patient, removed a section of skin from the abdomen, carefully wrapped the skin in a piece of paper and placed it in his pocket. Thirty-six hours later, for 19 of which the paper-covered skin was in Dr. Brewer's pocket, the graft was cut into five small sections and grafted on a healthy granulating ulcer of the right leg of a 38-year-old Irishman. Three out of the five sections were reported as "takes," and thus in 1881 one of the first skin "banks" was born.

Since this early experiment, skin has been stored in petrolatum, moist gauze, and pliofilm at refrigeration temperatures of 3 to 6 C. Carrel[8] proposed that these temperatures reduce cellular metabolic rates to a point of suspended or latent life.

At present these methods permit storage of skin for an average of two or three weeks. The clinical utility of stored skin is proportional to its length of storage, and therefore methods were sought which would increase the storage time. Hanks[9] had noted that the conventional methods did not consider the nutrient and excretory requirements of a slowed cellular metabolism at 3 C. In order to satisfy these requirements, he developed a buffered nutrient medium of 10% serum and a balanced salt solution. The pH changes brought about in the solution by cellular

5. Flosdorf, E. W.: Freeze-Drying, New York, Reinhold Publishing Corporation, 1949.

6. Kreuz, F. P., and others: A Comparison of Fresh Autogenous, Frozen, and Freeze-Dried Homogenous Cortical Bone Grafts, unpublished data.

7. Brewer, E. P.: On the Limit of Skin Vitality, Med. Rec. **82**:483-484, 1882.

8. Carrel, A.: The Preservation of Tissues and Its Application in Surgery, J. A. M. A. **59**:523-527 (Aug. 17) 1912.

9. Hanks, J. H., and Wallace, R. E.: Relation of Oxygen and Temperature in the Preservation of Tissues by Refrigeration, Proc. Soc. Exper. Biol. & Med. **71**:196-200, 1949.

metabolism were measured by a phenol-red indicator, which was added to the original solution. When a color change became apparent the nutrient solution was changed.

The solution was further modified by Dr. W. R. Earle and his group at the National Institute of Health. In this solution, the salt content and bicarbonate CO_2 buffering system differ from that proposed by Hanks. Human plasma has been substituted for serum because of its availability and the added buffering potential of fibrin. To control bacterial action, 50 units of both penicillin and streptomycin has been added. The modified solution is currently being investigated for the storage of skin.

Skin stored in these dilute plasma solutions was grafted in a series of 54 patients. Of these, 45 were ear, nose and throat patients and 12 orthopedic patients. Captain A. J. Delaney (MC), U. S. N., and his staff have used a total of 45 preserved homografts to line radical mastoidectomy and otofenestration operative cavities. It was estimated that after an initial take of 80% these grafts persisted three to five weeks. The homografts were stored for a minimum of three days and a maximum of 185 days. Twenty-six stored autografts were used in 12 orthopedic cases in which a physiological dressing was needed to cover large denuded areas resulting from trauma, such as battle wounds and frostbite. These autografts were the stored excess resulting from the initial split-thickness grafts, as suggested by Mathews [10] in 1945. The storage period of these grafts varied from a minimum of three days to a maximum of 84 days. Three stored homografts were used in orthopedic cases with a minimum storage time of 17 days and a maximum of 149 days. The average initial take for all types of skin grafts was 72%.

The temporary function of preserved skin homografts as a physiological covering may also be of value in treatment of traumatically exposed tendons, nerves, blood vessels, and extensive burns. Their use has been demonstrated to minimize pain, prevent plasma, red cell and electrolyte loss, and decrease purulent drainage and may even favor epithelization by restricting exuberant granulating tissue. When raw surfaces are covered with this material, the frequency and discomfort of dressings are reduced.

One of the major problems of this method of storage is that of accurate estimation of skin viability prior to grafting. Tissue culture has been proposed as a possible answer; however, we estimate that the majority of fresh skin implants in tissue culture fail to demonstrate growth. Therefore, this method has been temporarily rejected. At present, the only satisfactory method of determining viability is clinical observation following grafting of the stored skin on the patient. New approaches for determining skin viability are currently under investigation.

The problems of tissue processing and storage are paralleled by the difficulties of tissue procurement. Therefore, an operating room for sterile autopsy was established as an integral part of the tissue bank. This expedites efficient and rapid tissue procurement from fresh cadavers.

SUMMARY AND CONCLUSIONS

A tissue bank has been established on an experimental basis to develop methods of tissue procurement, processing, and storage.

10. Mathews, D. N.: Storage of Skin for Autogenous Grafts, Lancet **248**:775, 1945.

Fresh autogenous tissues retain their position as the ideal grafting material. However, under certain conditions the use of stored homogenous tissue is not only justified but desirable.

The sterile autopsy offers a possible solution to the major problem of tissue procurement.

Methods of tissue preservation are (*a*) freeze-drying for bone and (*b*) a refrigerated buffered solution of 10% plasma and balanced salt solution for skin.

Clinical and experimental results are encouraging; however, additional fundamental investigation is necessary.

ABSTRACT OF DISCUSSION

DR. PHILIP D. WILSON, New York: Dr. Hyatt has given us a good presentation of the technique that they are using at the Naval Medical School, and we are going to hear more about it. It is still at an early stage, but it is full of interest. I had the pleasure of visiting this school in April and seeing all the work which is being done and the facilities and equipment which are there. Dr. Hyatt and his associates, Dr. Kreuz, Dr. Turner, and Dr. Bassett, are doing excellent work.

I have had no experience at all with the use of dry frozen bone, nor have I had any experience with the use of preserved skin, but obviously if a technique can be worked out such as they describe for the preservation of bone and skin, it is going to be of great value not only to the armed services but also to civilian surgeons.

I should like to present a few slides showing our results with the frozen bone, because after all this is the older method. It is the one we know most about, and any new method has to be compared with the results obtained by this one.

[Slide] This is a complicated slide, concerned with 259 patients and 307 operations.

[Slide] There were 37 failures or 15%. You will see that bone cysts occurred. Eighteen of the lesions were pseudoarthrosis of the spine, seven were tuberculous lesions, two were osteomyelitis, and one was an effusion.

[Slide] In this group there were 14 infections. In six cases there was infection. Ten healed without loss of bone. These are important factors. The rate of success is 85%.

[Slide] These are just a few experimental results. In regard to the iliac graft, we found exactly what has been found by Anbott, Bost, and others in their group, namely, that cancellous bone heals much more rapidly than cortical bone. Here you see a plug. This is a trephine plug of the ileum, replaced with refrigerated iliac bone. You will see that at the end of two weeks the graft is already healed in place. At the end of three weeks it is practically solid. The center has not yet been revascularized, but you can see that there is rapid healing.

[Slide] Here are a few ulnar grafts that were resected. On one side you see the autogenous and on the other side the refrigerated graft. Here, after three weeks, there is practically no difference. There is a little defect, but you can see the appositional callus already forming rapidly at this time.

[Slide] This shows the type of experiment. Next is the picture after three weeks and then after six weeks.

[Slide] Here is a healing of the graft sections at the end of six weeks; the refrigerated graft is ahead in healing and much ahead in the amount of callus. There were individual variations, depending on the health of the animal.

[Slide] After 10 weeks the autogenous graft is ahead of the refrigerated graft.

[Slide] Here is an animal at 12 weeks. In none of these animals did we get healing of both ends of the graft. There was healing of one end but always nonunion at the other. That applied to both the autogenous and the refrigerated graft.

The point which I am making in showing these experiments is that it is dangerous to try to draw conclusions from experiments with bone unless you use a good experimental method. I have seen recently a number of reports of work being done with animals in which the graft that was being tested was placed in contact with the bone throughout the entire leg. I feel that

this is an erroneous method and that any conclusions drawn are likely to be inaccurate. You must have a considerable specimen of bone, with only end-to-end contact, so that you get a chance to see whether there is ingrowth of bone or whether there is any production of bone from the grafted segment itself.

DR. LENOX D. BAKER, Durham, N. C.: It has been a pleasure to hear this paper on the study of preserved tissues. Many orthopedic services are using bone banks. Undoubtedly banked bone has a useful place, and as more and more is learned about the preservation of tissues banked bone will assume a more important role in reconstructive surgery.

In the present state of knowledge on this subject it appears that the goal should be a method or process that will make it possible to preserve tissue in a living state or in a state in which the cellular structure of the tissue is unchanged.

Various methods have been proposed for the preservation of tissues. The greatest amount of work has been done with blood components and with skin, and because of the ease of securing and working with these tissues it probably will be in these fields that the greatest progress will be made.

It is hoped that what is learned will be applicable to bone. As pointed out by Dr. Hyatt, there is general agreement that the survival of skin stored at 2 to 6 C. is roughly inversely proportional to the length of time of storage. Freezing, according to the pioneer studies of Luyet, causes cell death through disruption of cellular architecture, rupture of cell membranes, and denaturization of protein. Luyet in his early work on vitrification used the vinegar eel and learned that by lowering the temperature sufficiently rapidly to avoid crystallization the eels could be held in the vitrified state for long periods of time without loss of life. The same findings have been seen in the study with bacteria.

In the course of experiments at the Duke University School of Medicine on the ultrarapid cooling of blood, it became obvious to Keeley, Gomez, and Brown that skin and similar thin tissues might be well suited to preservation through the process of vitrification.

The vitreous state may be described as a solid amorphous form of matter in which the molecules remain distributed at random without crystallization. Glass is a typical example. The process of crystallization requires time. So if the cooling velocity is sufficiently rapid, molecular movement is slowed or stopped before these molecules can arrange themselves in geometric patterns or in what amounts to crystals. Similarly, once a material is vitrified, a rapid velocity of rewarming is necessary for the material to retraverse this zone without cystallization. As long as a vitrified material is kept below the zone of crystallization, it will remain vitrified. The velocity necessary in the cooling and rewarming to prevent crystallization may be in the neighborhood of several hundred degrees centigrade per second, depending on the water content and the nature of the solute. For example, solutions containing 90% water would require extremely rapid velocities of cooling, whereas certain solutions containing only 30% water might not crystallize regardless of the cooling velocity.

With these principles in mind, Keeley, Gomez, and Brown took split-thickness grafts from dogs with the Padgett dermatome. The skin was divided into a number of 3-cm. squares and processed as follows. Several squares were dehydrated in sterile ethylene glycol for various periods of time ranging from zero to one minute. These dehydrated segments were ultrarapidly cooled by plunging them into liquid nitrogen at —196 C. The vitrified skin was stored at either —18 C. or —70 C. for varying lengths of time. These storage temperatures were chosen because preliminary studies had led them to believe that the devitrification temperature of skin is in the neighborhood of —14 C. Just prior to grafting, the vitrified segments were rewarmed rapidly by plunging them into isotonic sodium chloride at 40 C. Other sections of the same graft were allowed to freeze and, when stored, were kept at the same subzero temperature as the vitrified segments. In all cases immediate transplantation of unmodified squares was done to serve as normal controls.

Over 90% of the vitrified unstored grafts survived as permanent skin. Frozen skin, grafted simultaneously, died. In three dogs studied thus far, vitrified skin segments stored up to 45 days have survived as permanent skin.

The work of Keeley, Gomez, and Brown is cited as it is based on the principals of dehydration followed by rapid vitrification with the same general results as Captain Hyatt and his

co-workers have seen following the reversal of the process—that is, freezing followed by freeze-drying. The importance of this work cannot be overemphasized. Those interested should visit the exhibit that Dr. Hyatt and his co-workers are presenting in the scientific exhibit hall.

Dr. G. W. Hyatt (MC), U. S. N.: We are in full accord with the views expressed by Dr. Wilson and Dr. Baker. Before we accept the clinical utility of freeze-dried bone, we must have statistical comparisons which are the equal of those for frozen bone. I might add that we leaned heavily on the experimental and clinical work of Dr. Philip Wilson and Drs. Bush and Garber, for it was the success of their basic work which encouraged us in the experimental and early clinical use of freeze-dried bone.

Dr. Baker's discussion on the fundamental points of preserving tissue by freezing reemphasizes the importance of the ice crystal patterns. Preliminary observations of such patterns in frozen tissues by Dr. Merryman, Naval Medical Research Institute, indicates that tissues frozen below —120 C. have minimal formation of ice crystals. Warmer temperatures resulted in a growth of ice patterns. This would explain the mechanically deranged cellular architecture which we observed in bone stored at —20 C. Further, the growth of ice must come from tissue fluid, and as the water freezes the inorganic and organic salts become concentrated and may appreciably alter pH; this may denature tissue protein significantly. The associated gassing may insulate the tissue and further impair an even rate of freezing.

Liquid nitrogen does give a quick freeze. Since tissue substance is not homogenous, the coefficient of expansion may vary enough to damage tissue. We have actually cracked blood vessels while freezing with liquid nitrogen.

Dr. Baker's comments about the process of dehydration preliminary to freezing are noteworthy. If the tissue is not damaged appreciably in the initial drying, we have come a long way. The damage from ice formation may be minimized by making less solution available to form ice. Tissues processed in this manner must be stored at low temperatures. We feel that freeze-drying may be of value to us clinically because we can store and ship at ordinary temperatures.

LOCAL HEMOSTASIS IN THE HEMORRHAGIC SYNDROME OF IRRADIATION

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IN AN EARLIER experiment [1] we demonstrated the efficacy of gelatin sponge in controlling local bleeding in the presence of the coagulation defect produced by controlled heparin and bishydroxycoumarin (dicumarol®) therapy. We had the impression that the fine mesh of interstices in gelatin sponge was responsible for the hemostasis, since the sponge was effective regardless of whether the fibrinogen phase or the prothrombin phase of coagulation was altered.

In the present experiment we have produced a hemorrhagic syndrome in dogs with large doses of total body x-irradiation in order to test the effectiveness of gelatin sponge in controlling local bleeding in the presence of the complex coagulation defect due to irradiation.

METHODS

Sixteen mongrel dogs weighing from 6 to 9 kg. were used in this experiment. Dogs were dewormed and one week later subjected to total body irradiation,[2] 350 to 400 r, while under intravenous pentobarbital sodium anesthesia.

Preirradiation laboratory tests included a platelet count by the Rees-Ecker method and determination of the total white blood cell count and the coagulation time.[3] These tests were repeated 8 to 11 days after irradiation (Table).

From the Department of Surgery, Northwestern University Medical School.

Valuable assistance was given by Marvin V. McClow, M.D., Department of Radiology.

1. Laufman, H.; Preston, F. W., and Bourdeau, R.: Efficacy of Hemostatic Agents in the Presence of Anticoagulant Therapy, A. M. A. Arch. Surg. **63**:60-69 (July) 1951.

2. Irradiation was given with a 220 kvp machine, the physical factors being 220 kv, 20 ma, 0.5 mm. Cu, 1 mm. aluminum filter, and target skin distance 150 cm. With these factors, the r per minute in air was calculated at 4.22. This was verified by ionization chamber measurements in air at the center and at the periphery of a 20 in. (50 cm.) diameter field. The "fall off" from the center to the periphery was found to be less than 10%. Dogs were irradiated in the lateral decubitus position with the entire body within the 20 in. diameter field. Ten dogs were given the entire exposure in the left lateral decubitus position, and six dogs were given one-half the total exposure in the left lateral and the second half in the right lateral decubitus position. The total time of irradiation was 82 to 95 minutes, giving a dosage of 350 to 400 r in air. Dogs were irradiated in pairs.

3. Whole blood clotting times were done as follows: 8 cc. of blood was drawn by clean femoral venipuncture or by femoral vein "cut-down" into a siliconized 10 cc. syringe, using a No. 18 needle. Timing for coagulation was initiated with the first appearance of blood in the syringe. With as little disturbance as possible, the syringe was disconnected from the needle and 1 cc. of blood discharged from the syringe into each of three clean, dry, nonsiliconized culture tubes measuring 8 mm. (internal diameter) by 75 mm. (length). Ten minutes after the initiation

Ten of the 16 dogs showed a coagulation defect evidenced by a whole blood clotting time of 49 to 95 minutes, compared with control levels of 14 to 28 minutes. Six of the 10 dogs were operated on during the period of prolonged coagulation. Of the remaining four dogs, three died spontaneously, while the fourth was used for blood studies.

Surgery was performed on four of the animals under intravenous pentobarbital anesthesia and two under local anesthesia. The spleen was exteriorized through a midline abdominal incision. Small rectangular segments of equal size were removed from the anterior central portion of the spleen in a manner similar to that described by us previously.[1] In preliminary tests some splenic wounds were permitted to bleed spontaneously, thus serving as controls; however, the dogs died during surgery. Consequently, in the six dogs reported here all splenic wounds were promptly packed with gelatin sponge and covered with a gelatin sponge plaque supported by digital pressure for a few minutes. The spleen was then replaced and the abdominal wall closed in layers. After death the spleen was sectioned through the gelatin sponge for microscopic study.

RESULTS

In the 16 dogs operated on with coagulation times ranging from 49 to 95 minutes, gelatin sponge controlled splenic wound bleeding in every instance. In one dog with a coagulation time of 54 minutes bleeding was controlled at operation

Results of Laboratory Tests Before and After Irradiation

	Before Irradiation				After Irradiation				
Dog	r	White Blood Cells	Platelets	Coagulation Time, Min.	Day	White Blood Cells	Platelets	Coagulation Time, Min.	Survival After Surgery, Approximate Hr.
6.....	400	15,300	285,000	18	11	0	4,000	54	12
8.....	400	11,400	192,000	28	8	800	29,000	49	24
9.....	350	17,500	74,000	21	10	1,100	16,000	45	48
13.....	350	18,000	168,000	25	9	350	54,000	66	36
14.....	350	13,500	166,000	14	8	2,200	.....*	95	24
16.....	350	7,500	165,000	15	8	4,000	130,000	75	72

* Platelets unable to be counted because of clumping of red blood cells.

by the gelatin sponge, but about 100 cc. of liquid blood was found in the abdomen 24 hours after surgery. There was evidence of bleeding around all three gelatin packs.

Only 2 of our 16 dogs showed gross external evidence of the hemorrhagic syndrome, one in the form of periocular purpura, wound hematoma, and vaginal bleeding, and the other in the form of oral hemorrhage (pulmonary). The low incidence of external manifestations of the hemorrhagic syndrome in our dogs was probably due to the fact that the postoperative survival period was short (12 to 72 hours after surgery), death occurring before external evidence of bleeding could become manifest.

Internal bleeding, on the other hand, was found in most of the animals. At autopsy 10 of the 16 dogs showed hemorrhagic pulmonary consolidation, while

of timing one of the tubes was tilted slightly. If the blood was liquid it was subsequently tilted at 1 minute intervals until coagulation had occurred, as evidenced by failure of the blood to flow upon complete inversion of the tube. When the blood in the first tube tested had clotted, a second tube was similarly tilted and, likewise, a third tube. The clotting time was determined as the time elapsed from the appearance of blood in the syringe until the blood in all the tubes had coagulated. Usually, though not always, the blood in the third tube tested remained fluid for the longest period of time.

5 showed gastrointestinal hemorrhage. Two of the 10 dogs with pulmonary hemorrhage had received terramycin orally twice daily from the day of irradiation until death, while two other dogs in this group received procaine-penicillin, 300,000 units intramuscularly, on the sixth to ninth and eighth to tenth days after irradiation. Three of the 5 dogs having gastrointestinal hemorrhage had received procaine-penicillin, 300,000 units intramuscularly, 6 to 9 days after irradiation in one instance and 8 to 10 days after in the other two.

COMMENT

The postirradiation coagulation defect is not completely understood. Allen [4] recently has stated: "The hemostatic mechanism is more complicated than can currently be explained and the damages produced by total body x-irradiation are only partly known. Rational and complete treatment of irradiation hemorrhage cannot yet be established." Our experiments indicated that at least local bleeding can be controlled by means of gelatin sponge in animals subjected to total body irradiation.

It is obvious to us that the local control of bleeding at surgery in irradiated animals is only a small step in the distance which must be traveled experimentally before it becomes possible to operate successfully on animals and human beings exposed to total body irradiation. Irradiated animals tolerate anesthesia and surgery extremely poorly. Even with the use of local anesthesia a laparotomy incision usually results in the death of an irradiated animal within 72 hours. The cause for this extreme brittleness is not altogether clear today. The large amount of current research in this field has made us aware of certain defects which can be expected to follow total body irradiation. These include thrombocytopenia, leukopenia, vascular damage, and prolonged coagulation.

As can be seen from the table, there is an unusually close correlation between survival time after surgery and the degree of leukopenia and thrombocytopenia imposed by the irradiation injury. For example, the animal (Dog No. 6) in which no leucocytes could be found and whose platelets numbered only 4,000 survived only 12 hours after operation. By contrast, the animal (Dog No. 16) whose leucocyte count was 4,000 and whose platelet count was 130,000 survived 72 hours postoperatively. Although coagulation time was prolonged in each of the six animals listed in the table it will be seen that there is no correlation between the coagulation defect on the one hand and either thrombocytopenia or leukopenia on the other.

If we are to find a means of successfully operating on irradiated subjects, certain questions must find clarification in future experiments. The question arises as to what dosage of total body irradiation is compatible with survival after postirradiation surgery. The dosages used in our experiments are ordinarily considered lethal, and yet animals irradiated to this extent would be expected to survive considerably longer than they did after operation. Unquestionably, with smaller doses of irradiation successful surgical procedure might be accomplished. The dosage would

4. Allen, J. G.; Moulder, P. V.; Enerson, D. M.; Lathrop, K. A., and Sanderson, M. H.: Summary of Irradiation Effects on the Blood Coagulation Mechanisms, in Abnormal Bleeding, Progress Report, edited by J. G. Allen, Argonne National Laboratory, March, 1950, Part 12, pp. 148-167.

naturally vary between animal species, since species variation in the LD_{50} following irradiation is known to be remarkable.

The question regarding certain types of auxiliary treatment which might make surgery more successful in irradiated animals was not investigated by us except that we did employ antibiotics in a few instances. Large doses of antibiotics in a few of our animals did not noticeably prolong their lives. It has been shown recently [5] that rutin will successfully control postirradiation capillary fragility to a certain extent. Certainly this finding requires further investigation for its possible influence on the success of postirradiation surgery.

We feel that it is important to note that we had no difficulty in controlling bleeding from an ordinary incision in the dogs operated on even without the use of gelatin sponge. Variations in bleeding activity within a wound could not be correlated with whole blood clotting time, platelet count or leucocyte count, or any combination of these features. Arterial blood pressures immediately prior to and after surgery were normal. The paradox of hypocoagulability in the presence of clotted blood and fibrin in the same animals has been commented on by Tullis.[6] Cronkite [7] observed firmly clotted blood in the renal pelves as well as microscopic fibrin in the lungs, intestinal ulcerations, and some blood vessels of goats and swine with incoagulable blood just before death due to exposure to atomic irradiation. Autopsies were performed on these animals immediately after death. Vitamin K does not prevent the hemorrhagic syndrome.[8] Whole blood transfusion does not restore blood coagulation in these animals.[8] Investigators agree that prothrombin activity as measured by the one-stage test remains within an effective range in most dogs subjected to massive irradiation.[9] This would imply an adequate level of accelerator globulin. In some dogs there is a terminal fall in prothrombin activity. Allen [8] restored the plasma of irradiated dogs having a reduced prothrombin activity to a normal prothrombin activity by incubation with protamine sulfate or toluidine blue prior to testing. We did not treat any of our animals with toluidine blue or protamine sulfate. Nonetheless, the question arises as to whether treatment with these substances might contribute to survival in postirradiation surgery. However, Allen has pointed out [10] that the increase in protamine titration in some dogs exposed to 450 r did not necessarily parallel the whole blood clotting time. From

5. Griffith, J. Q., Jr., and Couch, J. F.: Inhibition by Rutin of Radiation Injury to Capillaries, Blood **6**:552, 1951.

6. Tullis, J. F.: The Response of Tissue to Total Body Irradiation, Am. J. Path. **25**:829-852, 1949.

7. Cronkite, E. P.: The Hemorrhagic Syndrome of Acute Ionizing Radiation Illness Produced in Goats and Swine by Exposure to the Atomic Bomb at Bikini, 1946, Blood **5**:32-45, 1950.

8. Allen, J. G.; Sanderson, M. H.; Milham, M.; Karschon, A., and Jacobson, L. O.: Heparinemia (?) An Anticoagulant in the Blood of Dogs with Hemorrhagic Tendency After Total Body Exposure to Roentgen Rays, J. Exper. Med. **87**:71-86, 1948.

9. Cronkite.[7] Allen and others.[8]

10. Allen, J. G.; Moulder, P. V.; Sanderson, M. H., and Egner, W. M.: Some Observations on the Relationship of Heparin to Protamine Sulfate and the Blood Platelets, in Abnormal Bleeding, Progress Report, edited by J. G. Allen, Argonne National Laboratory, March, 1950, Part 4, pp. 34-59.

the standpoint of our experiment it is interesting to note [11] that Allen reported only slight in vitro antiheparin activity for gelatin, while in vivo gelation almost equaled protamine as an antiheparin.

SUMMARY AND CONCLUSIONS

In 10 of 16 dogs exposed to irradiation, 350 to 400 r, a hemorrhagic syndrome developed from 8 to 11 days later, as evidenced by prolongation of the whole blood coagulation time to 49 minutes or more.

Six of the 10 dogs were operated on and segments of tissue were removed from the spleen in each dog. In all six dogs the bleeding from these wounds was effectively controlled by packing with gelatin sponge. In one instance there was slight seepage.

Bleeding from the spleen and the abdominal wound was considered no more profuse than that encountered in normal dogs. The paradox of this finding in the face of a marked coagulation defect is discussed.

The fact that local bleeding can be controlled in postirradiation surgery may contribute in a small way to the eventual success in this field. Our findings imply that gelatin sponge will control bleeding regardless of the nature of the defect imposed on the coagulation mechanism. A large field remains to be explored regarding ways and means of successfully operating on irradiated subjects with some prospect of a successful outcome.

11. Allen, J. G.; Sanderson, M. H.; Egner, W. M.; Lathrop, K. A.; Enerson, D. M., and Moulder, P. V.: The Anti-Heparin Activities of Protamine Sulfate, in Abnormal Bleeding, Progress Report, edited by J. G. Allen, Argonne National Laboratory, March, 1950, Part 6, pp. 69-87.

BLEEDING FROM THE NIPPLE

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IN RESTRICTING this discussion to the management of patients having a bloody discharge from the nipple, I am attempting to focus attention on this problem to the exclusion of other important related matters such as the nonsanguineous discharges. It is in the handling of the bleeding nipple in particular that both the patient and the physician often pursue either an uneasy radical course or an uneasy conservative course. I refer specifically to the rather widespread use of amputation of the breast, usually a simple amputation, for this condition. And I refer, on the other hand, to that advice which is sometimes given to wait an arbitrary period of time or for the development of a mass, before deciding on a definite course of therapy.

It is no wonder that patients with this condition are concerned when all lay cancer literature warns particularly and properly about the appearance of any strange bloody discharge. And it is no wonder that the physician who sees only an occasional case of this type is confused by the conflict of authoritative advice and by the complicated diagnostic measures which have been suggested.

It is my present contention that some of these patients having such a bloody discharge need a radical amputation, some need a simple breast amputation, some need a partial or wedge resection, and some need the removal of a small area only. These various needs can be properly differentiated with a high degree of certainty. The differentiation is made by regular physical examination and, when the result of that is uncertain, by surgical biopsy, just as is commonly done in cases of a mass in the breast without bleeding. The unique problem here concerns the need of exploration and biopsy when a mass is not palpable.

PATHOLOGIC PROCESS

Some of the principal entities responsible for mammary bleeding are trauma, miscellaneous malignant tumors, including malignant duct papillomatosis, benign intraductal papilloma, chronic cystic mastitis with duct hyperplasia, chronic inflammation, and perhaps some general glandular disorders.

There is, of course, no difference of opinion about the conservative handling of traumatic lesions or about the radical handling of obviously malignant ones. However, in regard to most of the others, there is a difference of opinion as to what relation one bears to the other and what degree of malignancy is involved in each. It is easy to reason that hyperplasia of duct epithelium leads to papilloma of the duct and this in turn to papillomatosis of ducts or to simple encysted duct papillomas.

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It becomes more difficult to connect these with chronic cystic mastitis and adenosis of the breast. As regards all these points, there are various shades of understanding. It is commonly agreed that each lesion may undergo malignant change, but there is dispute as to just where the malignant process begins and where it is really present. For example, there are pathologists who feel that even the simple papilloma is a premalignant lesion and those who actually feel that it is Grade I carcinoma. On the other hand, most pathologists and surgeons have the feeling that such a papilloma is a perfectly benign lesion. It is no wonder that operations of various extent are done when they are based on such varying opinions regarding the underlying pathological processes.

These matters will p obably not be settled for some time. However, there are three observations which I should like to make.

The first concerns the question of the actual malignant nature of these small papillomas. If they are malignant, one would not expect so many cures from local removal of the lesion or even from simple breast amputation. Certainly in other malignant lesions of the breast the recurrence rate is discouragingly high even after radical amputation, yet all follow-up reports give nearly 100% cure in these cases by such localized removal.

The second observation concerns the actual local recurrence of papillomas or even of malignant lesions after local removal. My colleagues and I have not yet experienced such recurrence, and it is not too common. It is an ever-present possibility. We take the position in this matter that local removal of these papillomas is justified just as is the local removal of localized lesions of chronic cystic mastitis.

The third point concerns the theory that a great many malignant tumors have their origin in these small papillomas. While we have no weighty evidence one way or the other, it is apparent from our experience and records that relatively few patients with a malignant lesion of the breast gave any history of early bleeding from the nipple. In our series of cases bleeding from the nipple was a late development in advanced malignant lesions.

HISTORICAL OBSERVATIONS

An imposing array of authority can be quoted to substantiate both the affirmative and the negative answers to the question of whether breast amputation should be done in these cases of papillomatosis or when there is no mass palpable.

Bloodgood [1] was highly conservative, rendering the opinion that the bleeding nipple should be merely observed if no mass was palpable. Hart [2] reported satisfactory end-results after excision. Geschickter and Copeland [3] have expressed satisfaction with the local removal of single lesions. Miller and Lewis [4] adopted a conservative attitude, essentially that expressed in this paper. Adair [5] conceived

1. Bloodgood, J. C.: Benign Lesions of the Female Breast for Which Operation Is Not Indicated, J. A. M. A. **78**:859-863 (March 25) 1922.

2. Hart, D.: Intracystic Papillomatous Tumors of the Breast, Benign and Malignant, Arch. Surg. **14**:793-835 (April) 1927.

3. Geschickter, C. F., and Copeland, M. M.: Diseases of the Breast, ed. 2, Philadelphia, J. B. Lippincott Company, 1940.

4. Miller, E. M., and Lewis, D.: The Significance of Serohemorrhagic or Hemorrhagic Discharge from the Nipple, J. A. M. A. **81**:1651-1657 (Nov. 17) 1923.

5. Adair, F. E.: Sanguineous Discharge from the Nipple and Its Significance in Relation to Cancer of the Breast: A Study Based on 108 Cases, Ann. Surg. **91**:197-209, 1930.

these lesions as premalignant and advocated mild x-ray irradiation. This form of treatment now has no supporters. Snyder [6] took a conservative stand and recommended diagnostic surgery before amputation. In a paper reflecting one phase of the English attitude, Wakeley [7] made a "plea for conservative treatment without amputation." Currently, Haagensen and Stout [8] have advocated the conservative side, and Stout [9] has made the statement that "bleeding from the nipple is one of the rarest early signs of breast cancer and is a classical sign of intraductal papillary tumors."

On the other hand, Cheatle [10] unreservedly recommended a simple mastectomy in cases without mass. Wainwright,[11] after study of a small series, reluctantly came to the same conclusion. In an article published in 1941, Hinchey [12] felt "that the entire breast should be removed in these cases of nipple bleeding where no localized focus is clearly demonstrable. The bleeding breast with no tumor must be suspected of harboring not only a papilloma or precancerous epithelial type of hyperplasia, but even an actual impalpable carcinoma." In an article from the Mayo Clinic, Gray and Wood [13] gave clear evidence of strong belief that even the smallest papillary tumors are Grade I carcinomas, and, acting on that belief, performed simple mastectomies in almost all such cases. Estes and Phillips,[14] in reporting a series from the Scott and White Clinic, advocated simple mastectomy "for attempted cure of this condition as papillomata may be multiple in more than one duct and contrary to some authorities may become malignant."

DIAGNOSTIC PROCEDURES

The most helpful information can be obtained from the history and by direct physical examination of the breast by the usual methods of careful palpation and inspection. The finding of a definite mass is of greatest importance. One needs to make absolutely certain that there is a bloody discharge, and one needs to exclude some of the slightly colored normal discharges which are not bloody. It is necessary to be precise about the position of the orifice on the nipple from which the blood is being expressed. There are some 15 to 20 such orifices of the lactiferous tubules which are located in a circle around the edge of the nipple. Each one is at the apex of a pie-shaped section of the breast. The bleeding is ordinarily coming from only

6. Snyder, H. E.; Snyder, C. D., and Grosjean, W. A.: Benign Lesions of the Breast, South. Surgeon **16**:555-568, 1950.

7. Wakeley, C. P. G.: Duct Papillomata of Breast: Plea for Conservative Treatment, Brit. M. J. **1**:436-437, 1945.

8. Haagensen, C. D.; Stout, A. P., and Phillips, J. S.: The Papillary Neoplasms of the Breast: I. Benign Intraductal Papilloma, Ann. Surg. **133**:18-36, 1951.

9. Stout, A. P.: The Role of Pathology in Lesions of the Breast, South. M. J. **43**:208-212, 1950.

10. Cheatle, G. L.: Cysts and Papillomata of the Breasts, Brit. J. Surg. **9**:235-241, 1921.

11. Wainwright, J. M.: The Treatment of the Bleeding Breast, Am. J. Cancer **19**:339-352, 1933.

12. Hinchey, P. R.: Nipple Discharge: Clinicopathologic Study, Ann. Surg. **113**:341-356, 1941.

13. Gray, H. K., and Wood, G. A.: Significance of Mammary Discharge in Cases of Papilloma of the Breast, Arch. Surg. **42**:203-208 (Feb.) 1941.

14. Estes, A. C., and Phillips, C.: Papilloma of Lacteal Duct, Surg., Gynec. & Obst. **89**:345-348, 1949.

one of these orifices. Careful observation, therefore, gives reliable information as to the quadrant or section of the nipple, areola, or breast from which the blood originates. Localized pressure at various areas to exaggerate the flow of blood will give confirmatory information of this type. Transillumination of the breast is always mentioned as a method of aid in localization but in our hands has been of little assistance. Occasionally, however, the blood-filled duct near the tumor will stand out.

The cytological study of nipple secretions is an up-to-date method of evaluation. Jackson and Severance [15] thought well of the method but felt that "by no means should it supplant biopsy or other methods of diagnosis." Hertz,[16] of the National Cancer Institute in Washington, spoke of their persistent work along these lines, with questionably positive results in only a few of several thousand examinations. While further investigation along this line is highly important, it is at present definitely impractical for the clinical surgeon.

Radiographic localization by the injection of thin radiopaque solutions has been recommended by Hicken [17] and clearly shows a space-filling lesion in certain instances. In our hands, this is a tedious procedure which gives inconclusive findings and is time-consuming in the sense that an appointment with the patient and the x-ray department must be met. In addition it is criticized on the basis of adverse reaction in the event that the solution is misdirected outside of the duct. These maneuvers are carried on to the ultimate in technical manipulation by Leborgne,[18] of Montevideo, Uruguay, who has published a method of actual biopsy of a tiny tumor by the use of extremely delicate dilators, curettes, and alligator forceps by working through a duct orifice. It would appear to us that this procedure, while extremely clever, would have very limited application.

Unless a surgeon has a particular interest and experience in the subject, he is likely to join the group who feel that the bleeding breast might be malignant and that a simple amputation is the course to be followed for the peace of mind of all concerned and for the ultimate cure of the patient. As a matter of fact, this procedure may be too much or it may be too little.

CASES REPORTED

This report is based on the study of 44 patients who had a bloody discharge from the nipple. No surface lesions are included. Thirty-one of the patients are from the University of Arkansas Hospital from 1940 to 1950, and 13 are from our private practice during the four years 1946 to 1950. Numerous statistical deductions which might be drawn are omitted here. We principally want to determine the matter of palpable mass in respect to diagnosis and treatment.

The 17 malignant tumors of the breast with bleeding nipple (see Table 2) include 16 from a total of 243 breast cancers at the University Hospital, an incidence

15. Jackson, D., and Severance, A. O.: The Cytological Study of Nipple Secretions: Aid in Diagnosis of Breast Lesions, Texas J. Med. **41**:512-514, 1946.

16. Hertz, R. H.: Personal communication to the author.

17. Hicken, N. F.; Best, R. R., and Hunt, H. B.: Discharges from the Nipple: Their Clinical Significance and Mammographic Interpretation, Arch. Surg. **35**:1079-1094 (Dec.) 1937.

18. Leborgne, R.: Intraductal Biopsy of Certain Pathologic Processes of the Breast, Surgery **19**:47-54, 1946.

of 6.5%, and one from a group of 97 at our office, an incidence of approximately 1%. Only one was a malignant papilloma. The other 16 were types such as scirrhous or comedo. In general, the cases at the University Hospital were more advanced, and it is our impression that bleeding from the nipple in outright malignant growths is a late development rather than an early one.

In respect to the cases of chronic cystic mastitis for which five simple mastectomies were done, it is impossible to say with certainty whether or not these

TABLE 1.—*Cases of Bleeding Nipple Divided on the Basis of a Palpable Mass*

	Clinic	Private	Total	%
Number of cases with a palpable mass	25	4	29	66
Number of cases with no palpable mass	6	9	15	34
Total number of cases with bleeding nipple	31	13	44	100

TABLE 2.—*Diagnosis and Treatment in 29 Cases of Bleeding Nipple and a Palpable Mass*

Malignant			
Cancer	17	Radical mastectomies	17
Benign			
Chronic cystic mastitis	7	Simple mastectomies	5
		Wedge resection	1
		Local resection	1
Fibroma	2	Radical mastectomy	1
		Local excision	1
Papilloma	3	Local excision	3
	12		12

TABLE 3.—*Diagnosis and Treatment of Fifteen Cases with a Bleeding Nipple and No Palpable Mass*

Malignant			
No cases	..	No cases	..
Benign			
Papillomas	13	Simple mastectomies	6 (clinic)
		Simple mastectomies	2 (private)
		Local excision	5 (private)
Duct hyperplasia	1	Local excision	1 (private)
Chronic infection	1	Local excision	1 (private)
	15		15

individual patients should or should not have undergone a simple mastectomy according to our current concepts. We suspect that simple mastectomies were done in some instances because of the presence of the bleeding nipple. Such a sign with mastitis does require consideration of simple mastectomy but does not demand it. The decision of whether to perform mastectomy should be based on the degree and extent of the mastitis together with any coexisting papillomatosis just as it would be if there were no bleeding from the nipple.

Certainly radical mastectomy for fibroma is to be deplored. The data illustrate some of the confused thinking on the subject of the bleeding nipple.

While we found no malignant lesions among our cases without palpable mass (see Table 3), we know for certain that such cases exist and must be constantly searched for.

The handling of the benign papillomas and the other nonpalpable lesions is the matter in which we are particularly interested. The performance of simple mastectomy in all six cases at our University Clinic reflects the rather general attitude toward this problem. The handling of two additional cases in the same manner among our private cases is along the same line. It was after the thorough study of the two breast specimens in these cases, in which we found only a small benign papilloma in one and a questionable papilloma in the other, that we became entirely dissatisfied with the procedure. Since that time we have performed local excision in the manner to be described and have been completely satisfied with it.

RECOMMENDED TREATMENT

It is obvious from the above observations that we lay great emphasis on the finding of a palpable tumor. When such is present the treatment is ordinarily directed in respect to the tumor just as though there were no nipple discharge. Some consideration has to be given to the possibility of there being two separate pathological entities present, such as a benign fibroma and a papilloma, one palpable and one not. It is in the cases in which there is no palpable tumor or in which there are one or more vaguely suspicious areas in one or both breasts that we recommend special handling.

A careful physical examination for localization of the position of the bleeding orifice is carried out. Ordinarily we employ none of the special examinations mentioned above because we find them of little practical assistance. We recommend a diagnostic exploration and biopsy of the bleeding breast or breasts. The procedure in itself is ordinarily a definitive one in the sense that the offending lesion is completely removed and nothing more needs to be done. These specimens are small and soft so that most pathologists prefer to base their final opinion on the study of permanent sections.

Surgical Procedure.—The procedure which we utilize is an extension of that well described by Davidoff and Freidman [19] in 1937 and by Babcock [20] in 1938 for the removal of palpable lesions beneath the areola. Undoubtedly this method has been used before that period. I think it is the method mentioned but not illustrated by Miller and Lewis [4] in 1923. It consists in a circumareolar incision made as short as possible though it may extend around half the circumference of the areola when necessary. This incision is made on the side where the bleeding has been noted. Local anesthesia suffices, and the procedure can ordinarily be handled on an outpatient basis. It is unnecessary to cannulate the duct as it can be readily seen beneath the areola when filled with blood.

It is not always necessary to elevate much of the areola or to disturb many ducts in order to find the lesion. However, if an extensive search is required, it is safe to separate the entire areola and nipple from the underlying tissues. This affords a

19. Davidoff, R. B., and Freidman, H. F.: The Treatment of Discharge from the Nipple, New England J. Med. **216**:1072-1074, 1937.

20. Babcock, W. W.: A Simple Operation for the Discharging Nipple, Surgery **4**:914-916, 1938.

Fig. 1.—Circumareolar incision used for widest exposure in the search for nonpalpable lesions causing bleeding from the nipple. A shorter incision is adequate for lesions just beneath the nipple or areola when they are palpable.

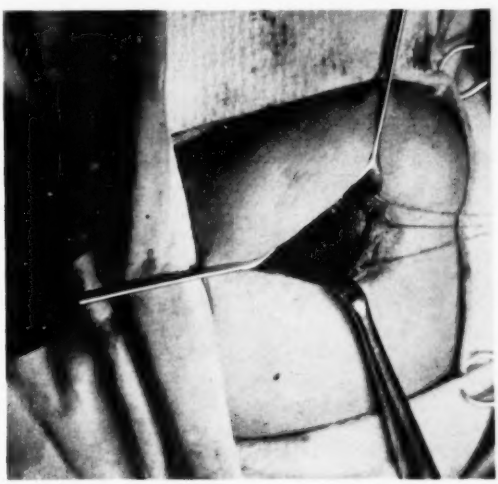

Fig. 2.—A papilloma deep within the central portion of the breast.

surprisingly fine exposure of the entire central core of the breast, where nearly all these lesions lie. There is adequate blood supply from the undivided half of the areola to retain viability in the entire areola.

Division of lactiferous ducts is theoretically undesirable and certainly disturbs later lactation. We have noted no other undesirable after-effects such as the formation of cysts. The situation is comparable to that of aberrant axillary breast tissue which has no system for external drainage.

If no blood-filled duct is immediately apparent, one needs to remember that the lesion may be very near the outlet of the duct, just beneath or almost within the nipple. If a short blood-filled duct is removed with or without a palpable small tumor in it and if nothing else abnormal is seen or felt, the surgeon should be content. This is probably all that would be found even if the entire breast were removed and extensively sectioned by the pathologist. If the blood-filled duct extends out into more solid tissue (and this finding is rare), a radial incision can be made and appropriate segmental resection done, based on the gross findings at operation. If there are found to be multiple blood-filled-ducts, multiple small cysts, or papillomas, a simple mastectomy can be done. If tissue is reported as malignant, radical breast amputation should be done with the knowledge that it is obligatory.

It has been our experience that dissection in this manner is sufficient to find and remove these simple lesions easily and with excellent cosmetic results. It affords the means of finding and removing representative tissue for microscopic study. The surgeon and pathologist may therefore take such action as they deem proper, based on this microscopic examination rather than on fear that there might be some hidden disorder present.

ABSTRACT OF DISCUSSION

Dr. William T. Fitts, Jr., Philadelphia: Dr. Hollenberg's excellent paper emphasizes the importance of individualized treatment of patients with a bleeding nipple, in contrast with treatment by a preconceived routine plan such as simple mastectomy, local excision or mere watchful waiting until the appearance of a mass. A recent study of 100 patients with nipple discharge at the Hospital of the University of Pennsylvania by Dr. Robert Horn, Jr., Dr. James Maxwell and me led us also to reject treatment by any single routine method.

Dr. Hollenberg limited his presentation to bloody discharge. In our experience a nonbloody discharge has almost the same significance as a bloody one. We believe that any discharge not associated with pregnancy or lactation is a sign of disease in the breast, the nature of which must be determined by surgical exploration. Although carcinomas of the breast that produce discharge are usually associated with a palpable mass, they may at times be occult, nonpalpable carcinomas. Within the past five years we have seen four patients in whom nipple discharge was the only clinical manifestation of a small, nonpalpable intraductal carcinoma. It is interesting that in one of these patients the discharge was serous.

The primary lesion in almost half of our patients was intraductal papillomatosis. A solitary papilloma was rare, and usually multiple gross and microscopic papillomas were found in a duct system. This observation leads us to the conclusion that the minimum operation constituting adequate treatment for papillomatosis is the resection of a pie-shaped segment of breast tissue from the nipple to the periphery of the breast encompassing the involved duct and its tributaries. But is such a limited excision justified in the presence of papillomatosis? Would not a simple mastectomy be safer? Most follow-up studies have shown that the development of carcinoma is rare after local excisions for papillomas but that it may occasionally occur. We have seen two instances in the last five years. The risk seems so small, however, that we believe partial mastectomy is justified for papillomatosis in most instances, especially in young women for whom the loss of a breast may involve considerable psychic trauma.

Almost all discussions of breast lesions point up how inexact are our methods of preoperative diagnosis. In an organ so susceptible to examination one would expect methods yielding a high degree of accuracy. The development of better methods of preoperative diagnosis is a real challenge to the physician.

DR. JOHN V. GOODE, Dallas, Tex.: It is easy for me to discuss this paper because Dr. Hollenberg and Dr. Fitts have expressed my opinion so exactly. All that is left for me to do is to emphasize some of the points they have made.

The first of these points is the rarity of bleeding from the nipple in cancer of the breast. In an experience of 240 patients with breast cancer, I have come across bleeding from the nipple only six times, and in those six instances the disease was far-advanced cancer and no problem in diagnosis arose.

The second point is that I believe intraductal papilloma occurs much more frequently than we realize, and the bleeding we see is only an event in the left history of the papilloma, probably toward the end when the papilloma is large and friable. In analyzing my cases I found 31 lesions that the pathologists considered intraductal papilloma, yet in these cases there was no discharge whatever from the nipple. There were 12 cases in which the discharge was bloody and 31 in which there was no discharge. For this reason I believe that papillomata exist much oftener than we realize.

The third point I should like to emphasize is the matter of frozen section on these delicate, soft, friable lesions. The pathologist should not be asked to give an opinion on a frozen section, because so often, in attempting to arrive at a definite diagnosis, he will use so much of the specimen that there is nothing left for paraffin section and a conclusive diagnosis. I think it is wiser to close the wound and let a permanent section be the basis on which the diagnosis is made.

If the disease process is such a diffuse one that partial resection will not remove it, then a complete resection of the breast should be carried out. The same is true whether the disease process is due to multiple adenomas, multiple cysts or bleeding from the nipple. If in operating for the one duct with the papilloma many ducts are found to contain blood, then it seems reasonable to me to give up that simple operation and remove the breast, because in no other way will one remove all the ducts that contain blood.

TREATMENT OF BILIARY DYSKINESIA WITH SPECIAL REFERENCE TO SPHINCTEROTOMY

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AND
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BILIARY dyskinesia is an elusive entity which is frequently overlooked as a cause for clinical symptomatology. The phrase means literally "a disturbance in the normal kinetics of bile flow." This disturbance can better be appreciated if the factors affecting normal bile flow are understood. The physiology of biliary dynamics is fairly well established. Bile secretion, which is a continuous process, is constantly being poured into the canaliculi of the liver.[1] The flow of bile depends on the vis a tergo of its secretory pressure (60 to 70 mm. of water) and is modified by the resistance offered by the sphincters in the biliary tract. These are located in the cystic duct, in the neck of the gall bladder and possibly in the hepatic duct.[2] Their presence is variable, and their function is uncertain, but they do not alter biliary dynamics materially. The important regulating mechanism of bile flow is the sphincter of Oddi. This is a complex structure which actually consists of a biliary, a pancreatic, and a variable ampullary sphincter.[3] It is the contraction of this sphincter mechanism which causes the primary obstruction to the flow of bile and increases the pressure within the biliary tree. The sphincter of Oddi is normally spastic in the fasting state and withstands a pressure of 100 to 150 mm. of water.[4] The normal secretory pressure of the liver (60 to 70 mm.) cannot overcome the resistance of the sphincter, and bile is therefore diverted into the gall bladder. However, the volume and pressure within this viscus are constantly reduced by fluid absorption. This concentrating power of the gall bladder acts as a pressure-regulating mechanism. The entry of the acid chyme into the duodenum causes a relaxation of the sphincter and simultaneous contraction of the gall bladder, with a free flow of bile into the intestine.[5]

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1. Best, C. H., and Taylor, N. B.: Physiological Basis of Medical Practice: A Text in Applied Physiology, ed. 5, Baltimore, Williams & Wilkins Company, 1950. Bockus, H. L.: Postgraduate Gastroenterology, New York, W. B. Saunders Company, 1950.

2. Mirizzi, P. L.: Physiologic Sphincter of the Hepatic Bile Duct, Arch. Surg. **41**:1325 (Dec.), 1940.

3. Bergh, G. S.: The Sphincter Mechanism of the Common Bile Duct in Human Subjects: Its Relations to Certain Types of Stimulation, Surgery **11**:299, 1942.

4. Doubilet, H., and Colp, R.: Resistance of the Sphincter of Oddi in the Human, Surg., Gynec. & Obst. **64**:622, 1937.

5. (*a*) Ivy, A. C., and Goldman, L.: Physiology of the Biliary Tract, J. A. M. A. **113**:2413 (Dec. 30) 1939. (*b*) Puestow, C. B.: Discharge of Bile Into the Duodenum: Experimental Study, Arch. Surg. **23**:1013 (Dec.) 1931.

If the sphincter mechanism fails to relax, the biliary tree becomes distended, resulting in pain or colic.[6] The etiology of this biliary dyskinesia is varied. It may be functional or organic.[7] The former type is prevalent in highly emotional women and may occur with the onset of menstruation. In others it may be associated with spastic colitis, asthma or other allergic conditions. The organic causes of sphincter spasm are probably secondary to biliary tract disease. The condition is analogous to pylorospasm, secondary to gastric or duodenal ulcer, or to spasm of the recto-sigmoidal sphincter, secondary to diverticulitis or carcinoma of the sigmoid. Actual inflammatory disease of the papilla,[8] recognized from hypertrophy and stenosis, may also be responsible for acute distention of the common bile duct. Finally, sphincter spasm may be caused by the increased concentration of acid in patients with hyperacidity and hyperperistalsis.

The clinical diagnosis of biliary dyskinesia, the symptomatology of which is almost identical with that of gall bladder disease, presents difficulties, especially in cases in which operation is not carried out. In some persons the relation of "gall bladder" attacks to nervous tension states or menstruation and the relief obtained by antispasmodics may suggest the diagnosis. In others a characteristic episode may be precipitated by a small dose of morphine which induces sphincter spasm. Oftener the diagnosis is made by exclusion and occasionally only by surgical exploration. If a normal gall bladder is found and no other disease is present, then dyskinesia of the sphincter must be considered. Under these conditions, cholecystectomy will aggravate the condition by removing the pressure-regulating mechanism. The notoriously poor results following cholecystectomy for mild noncalculous cholecystitis bear witness to this fact.[9]

Biliary dyskinesia as a clinical entity is recognized more frequently after cholecystectomy. It is the common denominator of the postcholecystectomy syndrome. In some series of cases as many as 40% of the patients have residual symptoms after cholecystectomy.[10] This is to be expected, because after cholecystectomy the mechanics of the biliary tree are disturbed. The loss of the pressure-regulating effect of the gall bladder and a spastic sphincter cause an increase in choledochal pressure resulting in discomfort and pain.[11] As time passes, the biliary ducts

6. (*a*) McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, J. A. M. A. **106**:2227 (June 27) 1936. (*b*) Puestow, C. B.: Changes in Intracholedochal Pressure Following Cholecystectomy, Surg., Gynec. & Obst. **67**:82, 1938. (*c*) Benson, K. W.: Dilatation of Bile Ducts and Its Relation to Stress After Cholecystectomy, Am. J. Digest Dis. **7**:1, 1940.

7. Hill, H. A.: Functional Disorders of the Extra-Hepatic Biliary System: Biliary Dyskinesia, or Dyskinesia, Radiology **29**:261, 1937.

8. del Valle, D., and Donovan, R. E.: Syndrome de colico provocado por fasciola hepatica, Arch. argent. enferm. digest. **4**:697, 1929.

9. Eliason, E. L., and North, J. P.: Morbidity Following Cholecystectomy, Ann. Surg. **109**:580, 1939. Ivy, A. C., and Sandblom, F.: Biliary Dyskinesia, Ann. Int. Med. **8**:115, 1934. Meyers, S. G.; Sandweiss, D. J., and Saltzstein, H. C.: End Results After Gall Bladder Operations, with Analysis of Causes of Residual Symptoms, Am. J. Digest Dis. **5**:667, 1938.

10. Doubilet, H.: Studies of the Biliary Tract in Relation to End Results of Operative Treatment, read before the Surgical Section, New York Acad. Med., 1943.

11. Judd, E. S., and Mann, F. C.: The Effect of Removal of the Gall Bladder, Surg., Gynec. & Obst. **24**:437, 1917. Puestow (footnotes 5 and 6*b*).

gradually dilate and the sphincter eventually loses it tonus. As a result, the symptoms of the postcholecystectomy syndrome usually subside within a few weeks or months with adequate therapy.

The treatment of biliary dyskinesia should be primarily medical. Careful study of the history of attacks in every patient will often disclose a precipitating situation or "trigger mechanism." This may be a specific emotional situation or a dietary indiscretion. These factors should be eliminated if possible. A regimen should be prescribed which will relax the sphincter and stimulate the flow of bile. This effect may be achieved by giving frequent small feedings and daily saline laxatives. In severer and more persistent cases, the "flush" treatment advocated by Best [12] has been employed, with good results. During an acute attack, the use of antispasmodics has been advised, and occasionally narcotics are necessary for relief. In cases associated with hyperacidity and hypermotility alkalis and parasympathetic drugs such as atropine and banthine® (β-diethylaminoethyl xanthene-9-carboxylate methobromide) should be used for treatment. If a spastic colon is present, the correction of constipation often relieves the symptoms.

However, in some patients the symptoms persist in such a severe form that surgical exploration must be advised.[13] The latter may reveal residual calculi in the choledochus or a remnant of the ampulla of the gall bladder or cystic duct. Occasionally a duodenal ulcer, previously unrecognized, accounts for the symptoms. Another contributing cause of the postcholecystectomy syndrome is recurring attacks of pancreatitis. In our experience this cause is infrequent. In a recent study by Dreiling [14] in which 137 patients suffering from the postcholecystectomy syndrome were tested by secretin, only three cases gave positive evidence of pancreatic disease and in two of these the diagnosis was proved by operation. The diagnosis of pancreatitis is made too frequently on the basis of symptomatology. Even a slightly elevated blood amylase level is not conclusive evidence of pancreatitis, and the presence of a communicating channel between the choledochus and the pancreatic duct does not necessarily indicate pancreatitis. Many patients in our series in which the common channel was demonstrated by injection of iodized oil have been followed for years and have never had a symptom which might be attributable to pancreatic disease. The secretin test should be used more frequently, for it yields valuable information as to function and disease. A clinical diagnosis of pancreatitis made by palpation is subject to a wide degree of error. A pancreatic biopsy, which may be performed without too great a risk, gives substantiating evidence, if positive. However in some cases no visible disease is found at operation to account for the severity of the clinical symptomatology. In instances such as this the diagnosis of dyskinesia of the sphincter must be entertained, and division of the sphincter should be considered for the relief of the symptoms.

Spasm of the sphincter of Oddi, with distention of the common bile duct as a cause of acute pain or colic, is often seen postoperatively in cases in which the

12. Best, R. R.: Quantitative and Qualitative Control of Bile Flow and Its Relation to Biliary Tract Surgery, Ann. Surg. **128**:348, 1948. Bettman, R. B., and Lichtenstein, G.: End Results Following Cholecystectomy, Am. J. M. Sc. **194**:788, 1937.

13. Colp, R.: Post Cholecystectomy Syndrome and Its Treatment, Bull. New York Acad. Med. **20**:203, 1944.

14. Dreiling, D. A.: Studies of Pancreatic Function: III. Use of the Secretin Test in Diagnosis of Patients with Postcholecystectomy Syndrome, Gastroenterology **16**:162, 1950; Personal communication to the authors.

T-tube has been clamped prematurely. Relief of pain is immediate with the free flow of bile drainage. When the sphincter spasm has been relieved, the T-tube may be clamped with impunity. These facts support the concept that dyskinesia of the sphincter is often a cause of severe clinical symptoms.

Many procedures have been proposed and performed for the relief of the sphincter spasm. One of the simplest is a gradual dilation of the sphincter of Oddi by suitable instruments. This is of transient value unless the dilation is forceful enough to divulse the musculature. However, this method is not without danger. It has also been suggested that the dilation of the sphincter be maintained by passing a long horizontal arm of a T-tube though the sphincter into the duodenum. Such a tube is left in situ for weeks or months. The effectiveness of this procedure is usually temporary. Others have attempted to bypass the sphincter by choledochoduodenostomy or choledochoenterostomy. Such procedures are frequently followed by eventual stenosis of the stoma and ascending cholangitis. Surgical division of the sphincter muscles is not a new procedure for the relief of pain and colic. It has been done for years. It is a necessity in the performance of transduodenal choledochotomy for the release of impacted ampullary calculi. It was done for sphincter spasm per se by Archibald,[15] Strode,[16] and others. However, prior to the introduction of chemotherapeutic agents and antibiotics, the occurrence of duodenal fistulas and peritonitis after anterior duodenotomy was not infrequent. For this reason an operation was proposed in which the sphincter was divided endocholedochally by means of a specially devised instrument.[17] It was felt at that time that this procedure was relatively safe and effective. Inasmuch as 14 years have elapsed since the procedure was first performed, we have reviewed our experience with endocholedochal sphincterotomy to determine the answer to the following questions: 1. Was the procedure always safe? 2. Was the diagnosis of biliary dyskinesia correct in those cases in which it was suspected, and did division of the sphincter give relief? 3. Were there recurrences of symptoms after this operation? The answer to these questions is the primary consideration of this presentation.

Tables 1, 2, and 3 represent the findings and results in 21 cases of endocholedochal sphincterotomy. All the patients in this group had symptoms so severe that they sought surgery for relief. At the time of exploration there were no visible pathologic findings to account for the symptoms. In four of the cases, Nos. 6, 11, 16, and 18, noncalculous disease of the gall bladder was found at the time of the primary operation. In five instances, Cases 3, 6, 10, 16, and 21, the sphincter of Oddi could be probed only with difficulty. In view of these findings and inasmuch as the pancreas appeared perfectly normal at examination, it seems reasonable to assume that a pathologic condition of the sphincter was the cause of the symptomatology.

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15. Archibald, E. W.: Personal communication to the authors.

16. Strode, J. E.: Biliary Dyskinesia from the Surgical Viewpoint, Ann. Surg. **117**:198, 1943.

17. Colp, R.: Treatment of Postoperative Biliary Dyskinesia: Report of 8 Cases of Endocholedochal Sphincterotomy, Gastroenterology **7**:414, 1946. Colp, R., and Doubilet, H.: Endocholedochal Sphincterotomy, Surg., Gynec. & Obst. **66**:882, 1938; Endocholedochal Sphincterotomy, with Report of 4 Cases, J. Mt. Sinai Hosp. **7**:334, 1941.

Thirteen patients (Table 1) have remained well for 3 to 14 years after endocholedochal sphincterotomy. At no time was there any evidence of pain, jaundice, ascending infection, or stricture. The results in five patients (Table 2) were not satisfactory. One was unrelieved of pain; two were benefited from 6 to 12 months after operation and then had recurrent attacks. In two the symptoms are milder than they were preoperatively, although the patients are not satisfied with the improvement. The period of temporary relief might be ascribed to a partial division

TABLE 1.—*Endocholedochal Sphincterotomy—Satisfactory Results (Thirteen Cases)*

Case	Previous Chole-cystectomy	Exploratory Findings		Period of Follow-Up, Yr.
		Common Bile Duct	Pancreas	
1	Yes	Normal	Biopsy, normal	14
2	Yes	Dilated	Normal	3
3	No	Dilated; stenosis of sphincter	Normal	11
4	Yes	Normal	Biopsy, normal	9
5	Yes	Dilated	Normal	8
6	Yes*	Dilated; stenosis of sphincter	Normal	9
7	Yes	Dilated	Normal	8
8	Yes	Dilated	Normal	5
9	Yes	Thickened	Normal	4
10	Yes	Dilated; stenosis of sphincter	Normal	5
11	No*	Normal	Normal	4
12	Yes	Dilated	Normal	3
13	Yes	Normal	Normal	3

* Noncalculous cholecystitis.

TABLE 2.—*Endocholedochal Sphincterotomy—Unsatisfactory Results (Five Cases)*

Case	Previous Chole-cystectomy	Exploratory Findings		Follow-Up
		Common Bile Duct	Pancreas	
14	Yes	Dilated	Normal	No relief
15	Yes	Dilated	Normal	Temporary relief
16	Yes*	Dilated; stenosis of sphincter	Normal	Relief for 1 yr., then recurrence with milder symptoms
17	Yes	Dilated	Normal	Relief for 8 mo., then recurrence of symptoms
18	Yes*	Normal	Normal	Well for 6 mo., then recurrence

* Noncalculous cholecystitis.

or trauma to the sphincter mechanism which resulted in a temporary paralysis. The recurrence of symptoms may be ascribed to a functional restoration of the sphincter mechanism. In Case 16, for example, a noncalculous gall bladder had been previously removed. The common duct was dilated, and there were definite stenosis and hypertrophy of the papilla at the time of exploration. The sphincterotome removed a piece of tissue which was reported by the pathologist as "hypertrophied sphincter" muscle. Postoperative cholangiograms revealed prompt entry of iodized oil into the duodenum, and morphine failed to produce any spasm. This case seemed to be a definite example of dyskinesia in which a good result was to be anticipated. The patient was relieved for almost a year and then symptoms recurred, although in

a milder form. The case strongly suggests the regeneration of an incompletely divided sphincter. There is also the possibility that in some of the cases in which there were unsatisfactory results the sphincter was not divided at all, that temporary benefit obtained may have been psychic in its origin, and that temporary relief may have been due to the dilatation incident to the passage of the sphincterotome. In others, the benefits of short duration may have been due to the division of adhesions, which later reformed.

Whatever the explanation, one must acknowledge the fact that a certain number of patients with apparent dyskinesia are not permanently relieved by endocholedochal sphincterotomy.

When sphincterotomy was first performed by us, in 1936, a duodenotomy was fraught with considerably more danger than it is today. Duodenal fistulas were not infrequent. The endocholedochal approach was devised because it was thought to be safer. Since the introduction of chemotherapy and antibiotics, and improved preoperative preparation, anterior duodenotomy has become much less hazardous.

TABLE 3.—*Endocholedochal Sphincterotomy—Errors in Diagnosis (Three Cases)*

Case	Previous Cholecystectomy	Exploratory Findings		Follow-Up
		Common Bile Duct	Pancreas	
19	Yes	Dilated	Normal	Died of carcinoma of pancreas 3½ yr. later
20	No	Dilated	Biopsy, normal	Died of carcinoma of ampulla 1 yr. later
21	Yes	Stenosis of sphincter	Normal	Died of secondary hemorrhage 2 wk. postoperatively; diagnosis, carcinoma (?)

Although our experience with endocholedochal sphincterotomy has shown it to be essentially safe, accidents are known to have occurred. There are other reasons, however, which favor the transduodenal approach. Errors in diagnosis may be reduced. In one instance, a periampullary carcinoma (Case 20) would have been recognized had a transduodenal approach been used. Moreover, the papillary region may be carefully examined, and a hypertrophied sphincter or inflammation of the sphincter can be definitely recognized. The sphincter may then be adequately and completely divided under vision, and hemorrhage, which is usually insignificant, can be controlled. Transduodenal sphincterotomy is a relatively simple procedure provided that the papilla is first identified by the passage of a probe, or a sphincterotome, through a choledochostomy stoma. After the complete division of the sphincter, the common bile duct is drained with a T-tube, one arm of the tube being introduced past the divided sphincter well down into the intestine. This precaution will reduce the possibility of a duodenal reflux. The clamped T-tube should not be removed for at least six weeks.

Since 1948, when endocholedochal sphincterotomy was abandoned, the transduodenal approach has been employed in 12 cases (Table 4). To date there have been no errors in diagnosis and only one recurrence of symptoms after this procedure. This was a case in which psychoneurosis was eventually proved to be the probable cause of the trouble.

The one fatality which occurred in this group was in the first patient in whom the procedure was performed. Death occurred 20 days postoperatively of hemorrhage from the gastroduodenal artery. Although the vessel may have been lacerated at the time of operation, it is more likely that secondary infection and ulceration about the divided sphincter and the adjacent duodenal wall were responsible, since bleeding did not begin until the seventh postoperative day. The relief of symptoms in the other 10 patients has been so marked that it must be attributed to transduodenal division of the sphincter. On the basis of our experience, we feel that exploration should be carried out when the postcholecystectomy syndrome is unrelieved by medical therapy and when the symptoms are severe and recurrent. If no organic cause is found to account for the symptoms, the sphincter should be divided, preferably by transduodenal approach.

TABLE 4.—*Transduodenal Sphincterotomy—(Twelve Cases)*

Case	Previous Cholecystectomy	Exploratory Findings: Common Bile Duct	Exploratory Findings: Pancreas	Follow-Up
22	Yes	Dilated	Normal	Well for 3 yr.
23	Yes	Dilated; stenosis of sphincter	Slight interstitial inflammation	Well for 2 yr.
24	No*	Normal	Normal	Well for 2 yr.
25	Yes	Normal	Biopsy, normal	Well for 1½ yr.
26	Yes* (no stones)	Dilated	Normal	Well for 1½ yr.
27	Yes	Dilated	Normal	Well for 1½ yr.
28	Yes	Dilated; stenosis of sphincter	Biopsy, normal	Well for 1 yr.
29	Yes	Dilated	Normal	Well for 1 yr.
30	Yes	Dilated; stenosis of sphincter	Normal	Died 20 days postoperatively of hemorrhage
31	Yes*	Normal	Normal	Well for 6 mo., then recurrence
32	Yes	Dilated	Normal	Well; recent
33	Yes	Normal	Normal	Well; recent

* Noncalculous cholecystitis.

SUMMARY

Biliary dyskinesia is a disturbance of the bile flow due primarily to spasm of the sphincter of Oddi. It occurs most frequently after cholecystectomy and is difficult to diagnose except by exclusion. In most cases the postcholecystectomy syndrome may be treated satisfactorily by medical measures. When surgical operation becomes mandatory, an organic cause is usually found to account for the symptoms. This may be a retained common duct stone or stump of the cystic duct. Pancreatitis is rarely a cause. When no organic disease is found, the symptoms may be ascribed to dyskinesia of the sphincter of Oddi. Division of the sphincter will relieve the symptoms in the majority of patients. Endocholedochal sphincterotomy was performed in 21 cases which were followed from 3 to 14 years. Because of recurrence of symptoms in five instances, due probably to incomplete division of the sphincter, and a mistaken diagnosis in three others, this procedure has now been replaced by transduodenal sphincterotomy. The latter has been employed for the past three years, with encouraging results.

CARDIAC MASSAGE IN THE TREATMENT OF ARREST OF THE HEART

A Study of Three Hundred Fifty Cases, with Two Original Case Reports

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THE SUDDEN appearance of cardiac arrest in an otherwise healthy person does not necessarily mean that the patient is already dead or that he is incapable of being restored to the more usual appearance of life. Where an overpowering insult, as anoxia, has caused the heart to cease contracting, it must be remembered that the rest of the body has not died, although the heart may seem to have done so, and that the heart itself can usually be made to beat again if proper measures are instituted with the utmost rapidity. Kountz studied the viability of human hearts after death, in the usual sense of the word, had already occurred; it was not his purpose to attempt resuscitation. He was able to revive 65 of 127 hearts; in some cases, death had occurred five and six hours before the bodies were obtained and revival attempted.

Sudden cardiac arrest appears most commonly during anesthesia and surgery. It may occur as a result of anesthesia through the mechanism of ventricular fibrillation, as a consequence of an overdose of the anesthetic agent, or as an effect of anoxia resulting from hypotension, respiratory obstruction, or respiratory depression, or it may possibly be due to a susceptibility to the depressant effect of anesthesia, amounting to an idiosyncrasy, known as status periculosus. Sudden cardiac arrest may occur in otherwise healthy persons in other circumstances, such as hanging, electrocution, asphyxia (as a result of respiratory obstruction), brain injury, shock, and injury to the heart itself. The idea of restoring to life persons who have apparently died under any of these conditions has fascinated investigators for many years; the conception of viability of the suddenly stopped heart and the execution of restoration find their greatest applicability during anesthesia and surgery. It has long been known that artificial respiration is required in these cases. Techniques applied to the heart itself have included puncture and massage; of these, the latter has proved more efficient. Starling (and Lane) published the first report of the successful use of cardiac massage in man. Igelsrud [1] may have successfully used the

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1. Green, T. A.: Lancet **2**:1708 (Dec. 22) 1906. Keen, W. W.: Therap. Gaz. **28**:217 (April 15) 1904. Mollison, W.: Brit. J. Child. Dis. **14**:42 (Jan.-March) 1917. White, C.: Surg., Gynec. & Obst. **9**:388 (Oct.) 1909.

technique in man a year earlier, in 1901. Schiff [2] had previously (1874) demonstrated the maneuver in dogs. Niehaus [3] is said to have been the first to attempt cardiac massage in man, in 1889.

CASE 1.—A 47-year-old white man received a tetracain (pontocaine®)-dextrose spinal block at 9:02 a. m. on June 7, 1950, for cholecystectomy. His preoperative blood pressure was 110/74; after the spinal anesthesia, it fell to 90/60 and then rose to 130/90. The operation was started at 9:13 a. m. At 9:20, because of pain or restlessness, administration of nitrous oxide was started. As the nitrous oxide was ineffectual, thiopental (pentothal®) sodium was administered at 9:32. At 9:40 the pressure was recorded as 90/60. At this point, after the third injection of thiopental, the patient, who until then had apparently not been sufficiently anesthetized to tolerate a pharyngeal airway, suddenly went into collapse. He appeared to be ashen gray and not deeply cyanotic. There was apparently no blood pressure or pulse. Fortunately, a needle had been inserted into a vein when he came to the operating room. Immediately, the following measures were taken: (1) The surgeon, feeling a quiet heart, began cardiac massage through the diaphragm; (2) a tube was inserted into the trachea, and artificial respiration was instituted and maintained with an anesthesia machine; (3) the head of the table was lowered, and (4) phenylephrine (neo-synephrine®) hydrochloride was injected intravenously. The effect of all these was dramatic. The patient's color improved, and the heart resumed spontaneous activity. At 9:50 a. m. the blood pressure was recorded as 150/94. The remainder of the operation was uneventful; the patient's tolerance to the artificial airway diminished as the dressing was being applied. He made a rapid and complete recovery. It had been noted, before beginning the anesthesia, that he seemed to be shivering as he was brought to the operating room.

The time from the discovery of the cardiac arrest to the beginning of heart massage was not more than one minute. After four or five manual compressions of the heart, it resumed spontaneous beating. The anesthetic, up to the moment of asystole, was administered by a resident.

CASE 2.—This case has been reported elsewhere (Cole) in somewhat more detail. A tetracaine-procaine spinal anesthetic was administered by the surgeon to a 21-year-old man, for inguinal hernioplasty, at 7:40 a. m. on June 21, 1950. During the next half hour the blood pressure fell, reaching 100/60 at 8:20. At 8:22 the patient's respirations and circulation ceased. Cardiac massage was begun through an abdominal incision at 8:27 and continued until 8:30. Epinephrine was injected into the heart at 8:31, spontaneous cardiac activity appeared at 8:33, and the patient resumed active respirations at 8:35. The incisions were closed at 9:20. The patient immediately became spastic; spasticity was soon followed by convulsions. I first saw him in consultation at 12 noon. He was unconscious, convulsing, and mildly cyanotic. Pulmonary edema was present; the rectal temperature was 105.2 F. A Guedel pharyngeal airway was inserted, and oxygenation was maintained with an anesthesia machine and face mask. I cooled the oxygen by immersing one of the breathing tubes in chipped ice and administered it under moderate pressure. The pulmonary edema soon disappeared. It was apparent that the patient was suffering from cerebral edema, in addition to his recent period of cerebral anoxia. Fifty cubic centimeters of 50% dextrose was given intravenously. At 1:30 p. m. 100 cc. of human serum albumin, containing 25 gm., was injected intravenously (Seldon and others). An equal amount was again administered at 3 p. m.[4] The convulsions did not appear again, and the patient's temperature immediately declined, reaching normal at about 10 p. m. He began to phonate the following morning. One hundred cubic centimeters of human serum albumin was again given intravenously. The use of oxygen was discontinued. He began to recognize people 48 hours after the cardiac arrest; at 53 hours he spoke intelligently and ate and drank easily. During the next two days he was disoriented and psychotic; after this, improvement began again. He first recognized me on the 10th day. Two days later, he exhibited a memory peculiarity consisting in his

2. Bost, T. C., and Neve, A.: Lancet **2**:552 (Oct. 26) 1918.

3. Vanpeperstraete, F., and Marion, C.: Anesth. et Analg. **7**:501 (Nov.) 1950.

4. The human serum albumin was supplied without cost by the American National Red Cross.

thinking he had done things twice that he had done once. This phenomenon quickly disappeared; his memory for recent events, which had become faulty, improved satisfactorily. He appeared to have made a complete recovery at the end of 23 days; he has since resumed all his former intellectual and physical activities.

Table 1 presents the results in 350 cases of cardiac arrest, in perhaps all of which artificial circulation was instituted by cardiac massage; individual listing would make too great a demand on space. The largest series of cases of cardiac arrest and massage until now have been reported by Bost (75), Bailey (40), Green (40), Norbury (15), Mollison (14), White (50), Keen (28), Cackovic (45), and Cooley

TABLE 1.—*Results in 350 Cases of Cardiac Arrest*

	Total	Recovered	Died	Recovery Rate, %	Mortality Rate, %
All cases	350	112	238	32.0	68.0
Valid cases	322	110	212	34.2	65.8
Five-minute cases	47	40	7	85.1	14.9
Five- to 15-minute cases	18	6	12	33.3	66.7

TABLE 2.—*Ten Cases of Recovery From Cardiac Arrest Treated by Massage of the Heart*

Time from Beginning of Arrest to Beginning of Massage, Min.	Time from Start of Arrest Until Beginning of Spontaneous Cardiac Activity, Min.	Operation	Anesthetic
..	35	Lobectomy	Endotracheal (Fauteux)
3	27	Repair of laceration of foot	Cyclopropane, drop ether (Fox; Lampson and others)
"Immediately"	20	Lobectomy	Endotracheal cyclopropane (Adams and Hand)
13	17	T & A	Chloroform and ether (Mollison)
8	10	Excision of epithelioma of chin	Chloroform (Fisher)
7 to 8	12 to 13	Cholecystectomy	Chloroform (Green; Mollison; White)
20	25	Cholecystectomy	Local, then alcohol, chloroform, and ether (Lee and Downs)
13 to 14	19	Appendectomy, not started	Spinal, pentothal (Thorek)
..	40	Pneumonectomy	Tribromethanol, endotracheal cyclopropane and ether (Touroff and Adelman)
4	86	Aortography	Pentothal (Owens)

(48). These numbers may not be added, since, as might be expected, many of these cases appear in two or more series and are sometimes identified only with difficulty. When the names of several investigators are repeated in the literature, as in the cases of Mauclaire, Gross and Sencert, and Gallet, in which no information is available to identify the various patients save that cardiac masssage was attempted without success in a case of asystole during anesthesia, I have eliminated all duplicate reports and have established that the actual number of cases presented here did occur. Three additional cases are not counted in the series, because of their resemblance to other cases, although the reports are not perfectly identical.

Ten cases are listed in Table 2, in which circulation, spontaneous or artificial, was absent for long periods of time and in all of which the patients made a complete recovery.

When respirations cease, the patient requires artificial respiration. There is no method of accomplishing this that is as efficient as using the anesthesia gas machine with its face mask (or better still, an endotracheal airway) and breathing tubes. When the heart has stopped, artificial circulation must be maintained; this is achieved only by cardiac massage.

The occurrence of apnea presents two problems: the maintaining of respiratory function (oxygenation and the removal of carbon dioxide) by any means, active or passive, and the instigation of spontaneous breathing. The first of these is more important than the second. Similarly, asystole poses two problems: the maintenance of circulation and the recurrence of spontaneous cardiac activity. Again, the first of these is the more important, for two reasons. First, it can be accomplished with certainty by the use of cardiac massage, when electrical stimulation and the injection of drugs do not often succeed and waste precious time. Second, once cardiac massage has been started, the emergency ceases to exist. The time interval that spells life or death for the patient is measured from the appearance of asystole to the institution of circulation; artificial circulation is effective. In Beck's words, the resuscitator, having started to perform cardiac massage, "began to move the blood by hand"; "to produce circulation by manual massage of the heart." No one would think of injecting drugs into an apneic patient instead of performing artificial respiration. Similarly, the patient in whom asystole has suddenly appeared should be given artificial circulation, by cardiac massage, rather than injections. Finally, just as artificial respiration, by taking advantage of the Hering-Breuer reflex, is instrumental in bringing about spontaneous respiration, it has been asserted (Vanpeperstraete and Marion) that cardiac massage has a specific stimulating action which tends to accomplish spontaneous cardiac activity.

When the blood pressure suddenly becomes unobtainable, it is extremely important to know whether or not the heart has actually stopped beating. I have seen no better discussion of this question than Bailey's.

> Those without practical experience of these catastrophes are inclined to pass this question by almost with contempt. . . . I have seen an already over-occupied anaesthetist burdened with this question when all the surgeon had to do was to remove a few abdominal packs and put his finger on the abdominal aorta. It should be obvious that if the operation in progress permits access to a large artery it is the surgeon who should inform the anaesthetist.[5]

The same investigator had an answer for those who condemn any one agent or technique in this connection: "I would also like to emphasise that experience has taught me that cardiac arrest can occur in any patient, with any anaesthetic agent, and with any anaesthetist."

Anesthetic agents employed in reported cases of cardiac arrest include alcohol, chloroform, cocaine, curare, cyclopropane, ether, ethyl chloride, ethylene, hexobarbital (evipal®) sodium, nitrous oxide, dibucaine (nupercaine®) hydrochloride, thiopental (pentothal®) sodium, procaine, stovaine, tetracaine (pontocaine®), tribromethanol, and trichlorethylene; posterior pituitary injection (or ergotrate®) was probably the precipitating factor in one case in which spinal anesthesia was used. Anesthetic techniques used in these cases have been brachial plexus block, endotracheal, face mask, insufflation, intravenous, local, open drop, rectal, spinal and topical.

5. Bailey, H.: Brit. M. J. **2**:84 (July 19) 1941.

In the past, the mortality rate in cardiac arrest has always been well over 50%. Orr, in his discussion of an article by Beck and Rand, said: "In the past seven years there have been 15 cases of cardiac arrest and resuscitation in the Lahey Clinic operating rooms. . . . Our survival rate at present is 46 per cent." Eversole stated a year later that the Lahey Clinic had 15 cases of cardiac arrest in the 12 years before 1950, in 8 of which the patient survived. These cases are regarded as a duplication and are not included in the series, although the mortality rates differ slightly. Topa and Dinischiotu stated in 1935 that Pieri had collected 20 successes in 76 cases. Pieri's cases have not been included here, for fear of duplication. Cackovic collected 45 cases in the literature, with nine recoveries; these cases are not included here, as most of them were reported elsewhere. Bost collected 75 cases, in 59 of which the patient died, a mortality rate of nearly 79%. White stated that "twenty per cent or ten were saved" of the 50 cases he reported. Bailey said: "I have performed cardiac massage about 40 times. In 13 cases the heart has restarted in earnest; but too often, after giving hope for hours or days, disappointment has been the outcome: only 4 patients have survived." Lee and Downs stated in 1924 that cardiac massage had "successfully resuscitated" about 25% of the patients recorded at that time. Vanpeperstraete and Marion collected 100 cases of cardiac arrest in the literature, although they said 180 cases had been published; there were 39 recoveries, but cardiac massage was the only resuscitating method in 21 or 22 of these patients. As the cases are not listed or identified, they have not been included in this series.

Of the 350 patients listed in Table 1, 112 recovered and 238 died, a mortality rate of 68.0%. The rate has been increased severely in this series by the inclusion of numerous unsuccessful attempts during the early part of this century, when it may be assumed that cardiac massage was not always performed promptly and efficiently. Keen said: "As nearly as can be judged (for some of the cases are rather vaguely referred to), massage of the heart has been attempted in twenty-seven cases. Of these twenty-four have been failures, and in three restoration has followed—a very meager showing so far, but not a surprising number of failures when the gravity of the condition is considered." Those cases in which the patient survived the ordeal on the operating table, only to die several days later of a condition definitely related to cardiac arrest, as right heart failure or pneumonia, are considered to be failures, for the purpose of calculating the mortality rate. White's case, in which death from tetanus occurred 11 days later, is regarded as a success in this connection.

A truer expression of the mortality is obtained by eliminating from the calculations those cases which obviously do not represent a valid test of cardiac massage in asystole during anesthesia, such as cases of hanging, electrocution, wounds of the heart, and laryngeal obstruction and cases in which it cannot be stated definitely that the heart was properly massaged. Of the remaining patients in this series, 110 lived and 212 died, a mortality rate of 65.8%. Thus, despite the readiness of older surgeons and anesthetists to pronounce death in the presence of sudden cardiac arrest, the statistical fact remains that the patient whose heart has suddenly stopped beating during anesthesia has about one chance in three of recovering completely if cardiac massage is performed. If it is done promptly, as in the more recent cases in this series, in which cardiac massage is known to have been started within five minutes after the heart had stopped beating, the survival rate may be as high as 85.1% (40 survivals in 47 cases), a far cry from "nulla pulsa, nulla therapia"

(White), indeed. Because of the inexactness of the term "immediate," cases so marked are not included in the last calculation. Note that in this series the recovery rate fell from 85.1% during the first five minutes to 33.3% during the next 10 minutes but that cardiac massage still revived one third of the patients.

I cannot insist that the actual mortality rate is as low as shown here. Few surgeons have the opportunity to perform cardiac massage more than once. There is little inclination to report a single unsuccessful attempt (although there are many such cases in this series), while a successful case is almost invariably published. I do maintain that the mortality rate of sudden cardiac arrest in the operating room is far less than is generally supposed when the heart is massaged; I have been able to collect 112 cases in which the procedure has been successful. Bost and Neve stated in 1918 that "it would be difficult to collect more than ten successful cases in the last ten years." Remember that some of the patients who died several days after operation would have died as a consequence of their original illness or of surgery, so that the mortality rate may actually have been unjustly increased by the necessity of counting every death.

When it has been decided that the heart is not beating, the patient will surely die unless something of a heroic nature is done for him and done promptly. Other procedures, such as intracardiac injection, defibrillation, countershock, and artificial pacemaker rhythm lack as good statistical support, require apparatus that is rarely available, and cannot be done promptly. Cardiac puncture is a dangerous procedure; the intracardiac injection of epinephrine is definitely contraindicated in the presence of ventricular fibrillation. Cardiac massage, as these cases indicate, is a lifesaving maneuver; it can be performed by any surgeon; it can be started in one minute; it requires no apparatus foreign to the operating room.

If the chest is opened to permit massage, the surgical pneumothorax makes endotracheal intubation mandatory; intubation is in any case advisable, since artificial respiration is required as urgently as is cardiac massage. If massage is performed through the abdomen, efforts at artificial respiration, however urgently they may be required, need be no different from what must in any case be done. Cardiac massage is surely the procedure of choice when the selection lies between itself, the usual temporizing intracardiac injections, and nothing. To avoid opening the abdomen or (what is far better but requires, at the same time, endotracheal intubation) the chest, while hopefully injecting epinephrine into the heart, is gambling with the patient's life with little expectation of success. To do nothing at all for the heart is, by modern standards, indefensible.

Only three cases could be found in the entire number of recoveries in which there were residual effects, the disturbance being very slight in one case, so that it may be said that almost invariably a patient who survives cardiac arrest recovers completely.

Too often, in the past, cardiac massage was resorted to only after considerable delay and when all other measures had failed, as they regularly did; the delay often exceeded half an hour. While we need no longer view the patient with sudden cardiac arrest in the operating room as being already dead, there are few emergencies in which time is as important as it is here. The patient's life is truly a function of the number of minutes during which he is without circulation, natural or artificial. If cardiac massage is performed within five minutes, six of seven patients with sudden cardiac arrest in the operating room can be saved.

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COEXISTING LYMPHOSARCOMA AND ULCER-CARCINOMA OF THE STOMACH

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THE SIMULTANEOUS development of a lymphosarcoma and a carcinoma in the stomach is exceedingly uncommon. Moreover, the supervention of a malignant lesion on a chronic peptic ulcer is of added interest. A search of the literature reveals the infrequency with which these lesions have been observed, diagnosed, and reported. Because of this rarity it seemed worth while to report a patient from the Jewish Hospital who at operation was found to have two lesions in the stomach, one a lymphosarcoma and the other a peptic ulcer undergoing malignant degeneration.

REPORT OF A CASE

I. F., a white man aged 64 years, was admitted to the Jewish Hospital with the complaint that for one year he had had attacks of left upper abdominal pains which also radiated to the back. The pain was not related to the taking of food. Bowel movements were regular until a year prior to his admission, when constipation developed alternating at times with frequent liquid stools. At no time did he have occult or fresh blood in the stools. He lost considerable weight during the past year.

Physical examination revealed a well-developed and fairly well-nourished man. The heart, lungs, and blood pressure were normal. The abdomen was soft, not tender and free from abnormal masses. The clinical impression was that the patient was suffering from a gastric ulcer.

Examination of the blood revealed a normal blood count and hemoglobin content. The blood sugar, urea, chlorides and proteins were within normal limits. The Mazzini test for syphilis was negative. Gastric extraction revealed no free hydrochloric acid and a total acid value of 6 units. The stools contained no gross or occult blood. Urinalysis disclosed sugar (4+).

Roentgen examination of the stomach after a barium sulfate meal showed the presence of an ulcer on the lesser curvature. In addition, the esophagus showed a diverticulum along the left lateral wall at the level of the carina. Barium sulfate could be demonstrated to pass into the trachea, indicating the presence of a tracheoesophageal fistula.

Laparotomy revealed two distinct lesions in the stomach. One lesion consisted of an ulcer measuring about 5 cm. in greater diameter; it was situated on the anterior wall of the stomach near the greater curvature, midway between the fundus and the pylorus. The second lesion measured 1 cm. in diameter and was located on the lesser curvature of the stomach about 4 cm. distal to the gastroesophageal junction. A very high subtotal gastrectomy and gastrojejunostomy was done; the patient made an uneventful recovery.

Gross examination of the specimen removed at operation disclosed two distinct lesions. The larger one consisted of a fixed tumor mass with an ulcerated mucosal surface and a puckered and indurated serosal surface. The other lesion found in the lesser curvature consisted of a circumscribed ulcer having sharp, punched-out edges (Fig. 1).

From the departments of surgery and pathology, Jewish Hospital.

Microscopic examination of the larger lesion seen on the anterior wall of the stomach presented a typical picture of lymphosarcoma. The tumor consisted of sheets and rows of cells which showed no definite structural pattern. The cells were of uniform size and shape, with little cytoplasmic substance. The nucleus was large, spherical, and hyperchromatic and occupied almost the entire body of the cell. Mitotic figures were numerous, denoting a high degree of malignancy (Fig. 2*A* and *B*).

Sections taken from the ulcer of the lesser curvature of the stomach showed in the main a characteristic picture of a callous ulcer. It consisted of a sharply cut breach of the epithelial surface bordering a crater which was floored with some necrotic material. Beneath this was a

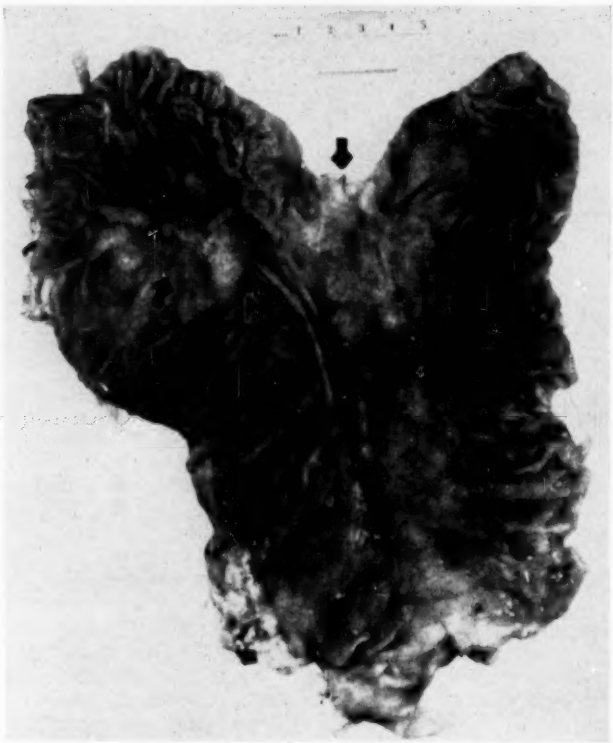

Fig. 1.—Photograph of stomach with one arrow pointing to the sarcoma and the other to the ulcer-carcinoma. The former is the larger of the two lesions.

mass of proliferating and partly organized fibrous connective tissue which extended right through the muscle coats of the stomach, completely interrupting their continuity. Embedded in the fibrous tissue were a number of blood vessels which showed in places considerable mural

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EXPLANATION OF FIG. 2

Fig. 2.—*A*, photomicrograph of lymphosarcoma: Hematoxylin and eosin stain; × 80. *B*, higher magnification of *A*. Hematoxylin and eosin stain; × 125. *C*, chronic peptic ulcer. Note organized fibrous connective tissue and cellular infiltration. Hematoxylin and eosin stain; × 80.

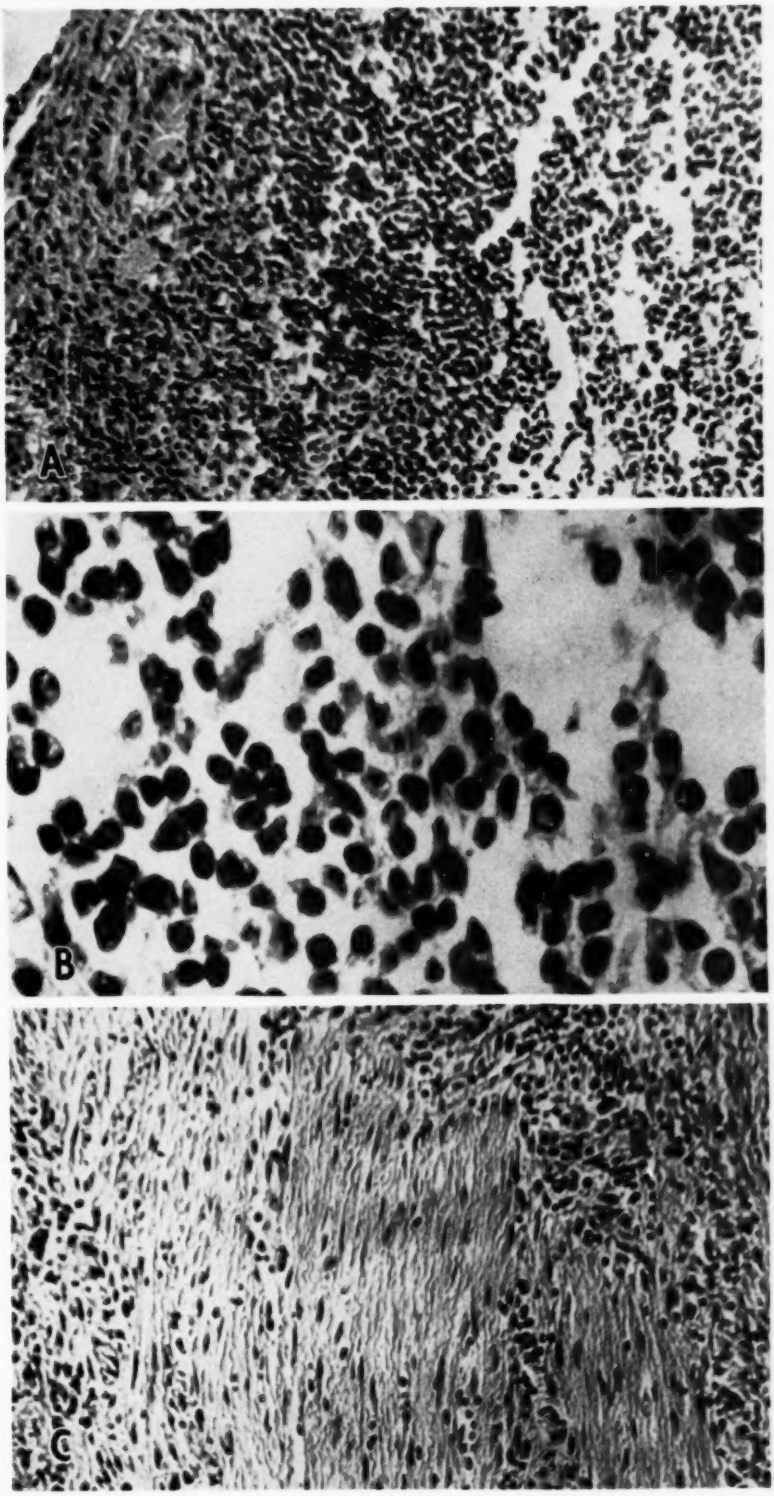

Figure 2

(See legend on opposite page)

thickening, with corresponding diminution in the caliber of their lumen. Occasionally, too, the lumen of the affected vessel was partly or entirely occluded by thrombus formation. The inflammatory cell reaction was of a chronic nature and consisted in a cellular exudate composed mainly of monocytes and to a less extent also of eosinophils, polymorphonuclear neutrophils and plasma cells (Fig. 2C).

Sections taken from the edge of the ulcer showed, in addition to the inflammatory process described above, an early carcinomatous formation. The cancerous growth consisted of large

Fig. 3.—Adenocarcinoma of the stomach engrafted on a peptic ulcer. Hematoxylin and eosin stain; × 80.

cylindrical cells containing a large hyperchromatic nucleus and arranged in nests or gland-like formations. It was apparent that the morphological character of the epithelium in this ulcer was changed from the normal and in places exhibited mitotic cell division. In areas close to the surface there was evidence of the first change from the normal to the abnormal epithelium, while at a point still farther down in the mucosa, the epithelium appeared definitely malignant and resembled an adenocarcinoma. At no place was the tumor seen to extend beyond the mucosal layer of the stomach (Fig. 3).

In summary, the stomach presented two distinct and independent lesions, one a lymphosarcoma and the other a chronic peptic ulcer undergoing malignant changes.

COMMENT

The simultaneous development of a sarcoma and a carcinoma in the same organ has been the subject of many theories and much criticism. Many hypotheses have been advanced to explain the development of such lesions, but as none are based on anything better than guess work they do not merit detailed discussion. It is not uncommon to find multiple tumor growths in the body, nor is it rare to find more than one tumor developing in a single organ. In the uterus, for instance, one may encounter the growth of a myoma and a sarcoma, or a sarcoma and carcinoma. In the stomach, however, the simultaneous growth of a sarcoma and a carcinoma is unusually rare. Schuback [1] described a tumor of the stomach consisting of both carcinomatous and lymphosarcomatous elements, while Götting [2] described a similar neoplasm in the stomach consisting of both spindle-cell sarcoma and carcinoma. According to these authors, the development of such mixed tumors is not readily explained. Virchow [3] recognized two groups of carcinosarcoma, namely, (1) endothelial, in which the same genetic cell gives rise to both sarcoma and carcinoma and (2) carcinomatous, the stroma of which is of a sarcomatous nature.

The lymphosarcomatous and carcinomatous growths noted in our case developed independently of each other and were located in portions of the stomach which were far apart. The tumor found in the anterior wall of the stomach was of a purely lymphosarcomatous nature, being composed solely of lymphoid tissue. Since lymphoid tissue is normally present in the stomach, one should expect to find a gastric form of lymphosarcoma. We [4] have described such tumors in the stomach in a previous communication. The carcinomatous tumor, on the other hand, was found on the lesser curvature of the stomach in close association with a peptic ulcer; the origin of this tumor is apparent.

The development of a carcinoma on a preexisting chronic peptic ulcer is of considerable interest. Divergent views have been expressed as to the relationship which exists between gastric ulcer and gastric carcinoma. It is hardly necessary to repeat the many statements which have been made with regard to the general question of the relationship of gastric ulcer to gastric cancer, as their trend is well known.

The best proof of the association of a peptic ulcer with carcinoma would be the development of carcinoma on a neglected ulcer or on an ulcer which has been under observation; this has been reported by numerous observers. Wilson and McCarthy,[5] of the Mayo Clinic, first popularized the idea in this country that a large number of cases which reach operation with a diagnosis of chronic gastric ulcer show malignant changes and that therefore the common fate of a gastric ulcer is the ultimate supervention of malignant changes. In the years that followed the pendulum of opinion with regard to the supervention of a malignant disease on a

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2. Götting, P.: Über Kollisionstumoren, Frankfurt. Ztschr. Path. **41**:107, 1931.

3. Cited by Götting.[2]

4. Rabinovitch, J.; Grayzel, D.; Swyer, A. J., and Pines, B.: Sarcomas of the Stomach, Am. J. Surg. **80**:550, 1950.

5. Wilson, L. B., and McCarthy, W. C.: The Pathological Relationship of Gastric Ulcer and Gastric Carcinoma, Am. J. M. Sc. **138**:846, 1909.

chronic ulcer has swung in the opposite direction. Spilsbury [6] pointed out that at the edge of a chronic ulcer we often find areas of distorted epithelium dragged down by scar tissue between the layers of muscularis mucosae and showing irregularities in the alveolar formation suggestive of early malignancy, though in fact they are benign. One of us (J. R.)[7] has observed similar changes in chronically inflamed gall bladder in which the surface epithelium has detached itself in places and has become buried in the deeper strata of the wall. Among these cells mitotic figures are often found and may give an erroneous impression of being malignant in nature. It is possible that such aberrant rests of distorted epithelium were regarded by the Mayo Clinic pathologists as early carcinoma. Stewart,[8] Dible,[9] and Morley [10] have also come to the conclusion that it is not the normal fate of a gastric ulcer to become malignant; nor is it unusual for a gastric cancer to originate in a chronic ulcer. In reviewing the material on gastric ulcer at the Jewish Hospital, we also noted that the incidence of carcinoma originating in a preexisting simple ulcer is low, being approximately 1.5%

It is evident that the casual association of ulcer with carcinoma of the stomach is uncommon. It is also evident that in a small proportion of cases of gastric cancers appearances are found which may point to the foundation of the growth on a preexisting chronic ulcer but that we cannot, in the majority of such cases, exclude the possibility that these appearances are produced either by distorted epithelial inclusions in the depth of the ulcerated wall or by the sclerosing character of the neoplasm. Allowing for these reservations, it is likely that peptic ulcers of the stomach may be considered the pathologic connecting link between benign ulcerative lesions on the one hand and carcinoma on the other but that it is in the small proportion of cases in which ulcers develop that carcinoma is likely to occur.

Klein [11] stated that in view of the frequent close similarity between a primary callous ulcer and ulcerated gastric carcinoma and the lack of any specific anatomic features which would indicate the preexistence of a benign lesion, an unequivocal pathologic diagnosis of ulcer-carcinoma is possible only in the few cases which can meet certain strict criteria. These criteria are that (1) the lesion must exhibit the characteristic features of a chronic peptic ulcer, (2) the malignant process must be localized to a narrowly circumscribed area of the ulcer margin, and (3) the ulcer base must be free of cancer or at least only slightly infiltrated adjacent to the focus of origin of the neoplastic growth. Obviously, this ideal picture may be observed only when the lesion is examined in its earliest stages of development. So far as our case is concerned, the ulcer on the lesser curvature of the stomach showed, in addition to the inflammatory reaction commonly seen in peptic ulcer, early carcinomatous formation. Furthermore, the transition from a simple inflam-

6. Spilsbury, B. H.: Morbid Anatomy and Histology of Gastric Ulcer, Proc. Roy. Soc. Med. **15**:25, 1922.

7. Rabinovitch, J., and Kieffer, R. S.: Squamous Cell Carcinoma of the Gall Bladder, Surg., Gynec. & Obst. **52**:831, 1931.

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9. Dible, J. H.: Gastric Ulcer and Gastric Carcinoma, Brit. J. Surg. **12**:666, 1924.

10. Morley, J.: Surgical Pathology of Ulcer and Gastric Carcinoma, Edinburgh M. J. **53**:273, 1946.

11. Klein, S. H.: Malignant Degeneration of Chronic Benign Gastric Ulcer, S. Clin. North America **27**:289, 1947.

matory process to a tumor which is morphologically and pathologically carcinomatous could clearly be demonstrated here. Undoubtedly, therefore, the carcinoma in this case was superimposed on a preexisting peptic ulcer.

The presence of two anatomically independent malignant lesions of the stomach is of great interest. Since such findings are not frequent, they attract great interest. A search through the literature reveals that the carcinosarcomas described in the stomach by various authors consisted of a single lesion which was made up of a mixture of sarcomatous and carcinomatous elements. In our case however, the stomach showed two independent tumor growths, one sarcomatous and the other carcinomatous. Furthermore, the carcinomatous growth was engrafted on a preexisting peptic ulcer.

SUMMARY

A case is reported in which a lymphosarcoma and a carcinoma were found as two independent growths in the stomach. Moreover, the carcinoma was engrafted on a preexisting peptic ulcer. The relative infrequency with which we find a carcinoma supervening on a chronic peptic ulcer of the stomach was cited from a short review of the literature and of the cases noted in the Jewish Hospital. Recognition of the pitfalls in the correct interpretation of lesions diagnosed as ulcer-carcinoma will greatly reduce the incidence of such cases.

EFFECT OF THE EXALTO-MANN-WILLIAMSON PROCEDURE ON GASTRIC SECRETION

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THE REGULAR production of progressive gastrojejunal ulcers in experimental animals when the alkaline juices of the duodenum are deviated into the intestinal tract lower down has been of great value in analyzing the pathogenesis of this disease and in evaluating certain forms of therapy. The commonly accepted explanation for the development of these ulcers holds that they are due to the digestant action of the pepsin hydrochloric acid of the gastric content coming in contact with intestinal mucosa, unprotected by the neutralizing and buffering action of the pancreatic juice, bile, and succus entericus. It is the purpose of the present communication to present data which indicate that a second, potent, ulcer-forming factor is set in motion, namely, a hypersecretion of gastric juice from the fundus and body of the stomach.

Exalto [1] was actually the first to produce experimental ulcers by this method and should be given full credit for this significant contribution. In 1911, while a resident surgeon in the University Clinic in Utrecht, Exalto was impressed with the fact that very few gastrojejunal ulcers occurred after a posterior, short loop gastroenterostomy by the method of von Hacker as compared with a large incidence of gastrojejunal ulcers in the Amsterdam Clinic, where an anticolic anastomosis of the "Y" type (the method of Roux) was commonly employed. Exalto theorized that the high incidence of gastrojejunal ulcers after the Roux type of operation might be due to the fact that the alkaline duodenal contents were drained away into the intestine lower down and did not come into contact with the anastomosis. He then performed the "Roux-Y" operation in dogs (Fig. 1) by closing the pylorus, dividing the upper jejunum, and anastomosing the distal end of the jejunum to the stomach. The proximal stump of the jejunum was then implanted into the jejunum at a lower level or into the colon. By thus deviating the bile,

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1. Exalto, J.: Ulcus jejuni nach Gastroenterostomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911; Ulcus jejuni na gastro-enterostomie, Nederl. tijdschr. geneesk. **5**:469, 1911; personal communication to the authors.

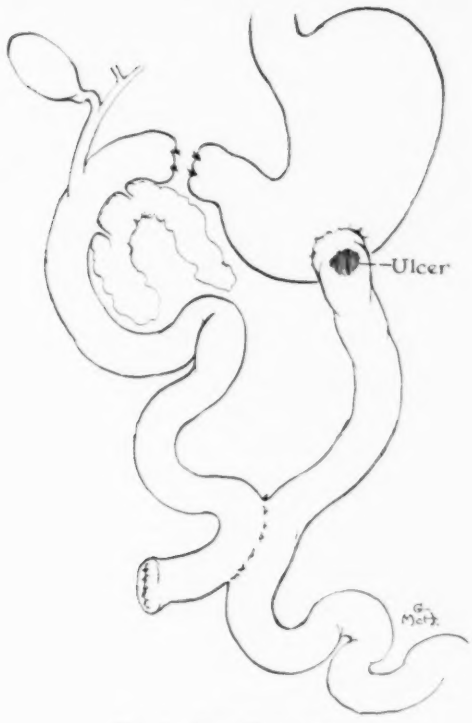

Fig. 1.—Roux-Y operation.

Fig. 2.—Mann-Williamson operation.

pancreatic juice, and succus entericus of the duodenum away from the gastrojejunostomy, he was able to produce marginal ulceration in a high percentage of his experiments. Similar studies were reported by Langenskiold [2] and later by Mann and Williamson.[3] The procedure which bears their names (Fig. 2) shunts the alkaline duodenal content into the terminal ileum and almost uniformly causes typical peptic ulcers to develop at the gastrojejunal stoma. These findings have been abundantly confirmed.[4]

The acid pepsin theory of ulcer genesis was further supported by experiments of Mann [5] and of Morton,[6] who were able to heal existing marginal ulcers which

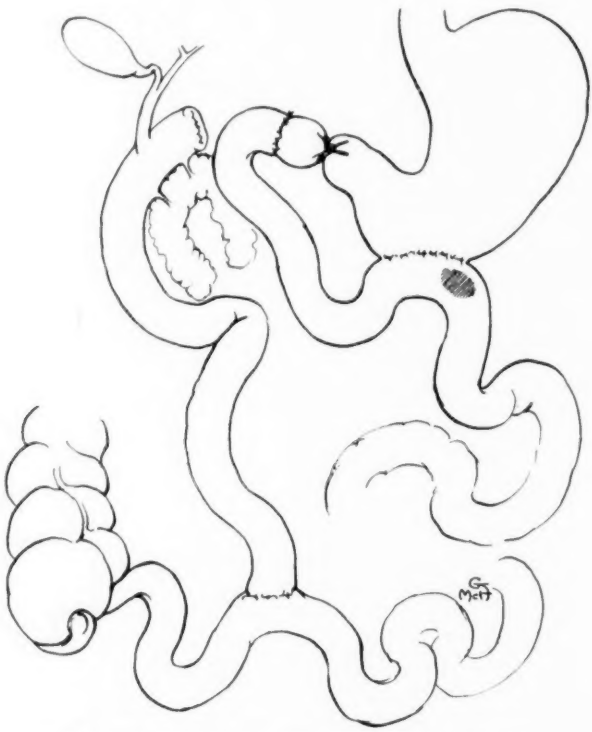

Fig. 3.—Mann-Morton operation for marginal ulcer.

2. Langenskiold, cited by Alvarez, W. C.: Light from the Laboratory on the Problem of Peptic Ulcer, Am. J. Surg. **18**:207, 1932.

3. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409, 1923.

4. Grossman, M. I., and Ivy, A. C.: Preparation and Use of the Mann-Williamson Dog, in Methods in Medical Research, edited by V. R. Potter, Chicago, The Year Book Publishers, 1948, Vol. 1, p. 263.

5. Mann, F. C.: Physiologic Mechanisms in Relation to the Development of Peptic Ulcer, Minnesota Med. **20**:755, 1937.

6. Morton, C. B.: Observations on Peptic Ulcer: Findings in Experimentally Produced Peptic Ulcer; Etiologic and Therapeutic Considerations, Ann. Surg. **87**:401, 1928.

had been produced by surgical duodenal drainage by performing a second gastrojejunostomy to divert the acid chyme away from the ulcer site (Fig. 3). Healing was also induced by performing a duodenojejunostomy opposite the ulcer site, thus neutralizing the acid of the gastric juice as it left the stomach. One of us, Dragstedt, with Matthews [7] modified the Mann-Williamson operation by draining the duodenal content into the jejunum 40 cm. below the gastrojejunostomy (Fig. 4). In only one of 21 animals operated on did a stoma ulcer develop. When a valve was

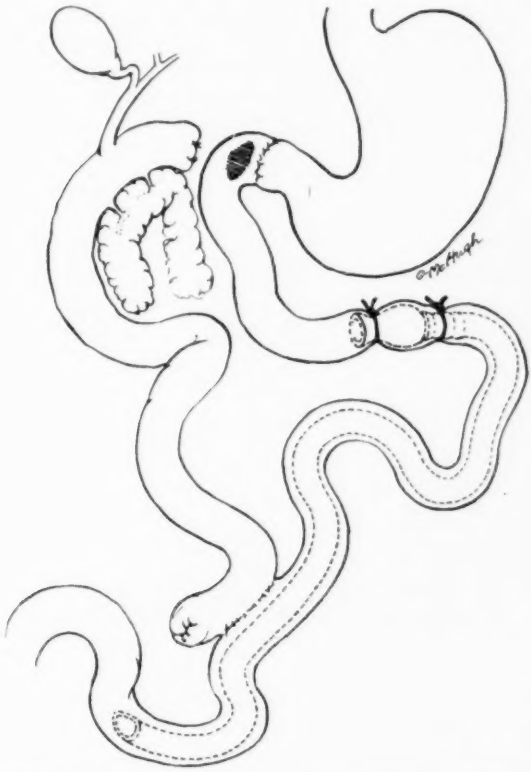

Fig. 4.—Matthews-Dragstedt modification of Mann-Williamson operation.

inserted into the jejunum between the two stomas to prevent regurgitation of alkaline juices, ulcers developed in 6 of 10 dogs.

On the basis of these experiments, it is reasonable to expect that diversion of the duodenal juices into the stomach would also protect against anastomotic ulceration, but this is not usually true. McCann [8] was able to produce typical ulcers in 80% of 26 animals operated on, as illustrated in Figure 5, where the alkaline juices

7. Matthews, W. B., and Dragstedt, L. R.: The Etiology of Gastric and Duodenal Ulcers: Experimental Studies, Surg., Gynec. & Obst. **55**:265, 1932.

8. McCann, J. C.: Experimental Peptic Ulcer, Arch. Surg. **19**:600, 1929.

of the duodenum were returned to the stomach. Ivy and Fauley [9] reported an incidence of 16% ulceration in 12 such preparations. We have repeated McCann's experiment and will present experimental evidence, which at least partially explains this paradox.

EXPERIMENTAL PROCEDURES

Intragastric duodenal drainage was performed in six dogs by the method of McCann, illustrated in Figure 5. Under ether anesthesia, the pylorus was divided and the duodenal stump closed. The first loop of jejunum was then transected and the proximal stump implanted into the gastric fundus, thus draining the duodenal content into the stomach. Intestinal continuity was reestablished by anastomosing the pyloric end of the stomach to the distal end of the jejunum. Two of the dogs succumbed to perforated marginal ulcers in 121 and 194 days, respectively. The other four animals, when killed after 165, 170, 171, and 283 days, displayed no

Fig. 5.—McCann method of producing experimental ulcer.

evidence of ulceration. Having confirmed the fact that marginal ulceration does occur despite intragastric duodenal drainage, an attempt was made to determine the reason for this phenomenon, which is of course contrary to the theory that the cause of the Mann-Williamson ulcer is the lack of neutralizing secretions at the stoma. To secure quantitative data concerning the effect of the Mann-Williamson procedure on gastric secretion, Heidenhain pouches were made, as illustrated in Figure 6*A*, with use of the watertight cannula collection method previously described from this laboratory. After an initial control period of gastric juice collection, intragastric duodenal drainage was superimposed on the Heidenhain pouch preparation, as illustrated in Figure 6*B*. After a study period of approximately two months, the duodenal content was diverted to the terminal ileum (Fig. 6*C*)—that is, the usual Mann-Williamson procedure was carried out. The effect of these

9. Ivy, A. C., and Fauley, G. B.: Factors Concerned in Determining the Chronicity of Ulcers in the Stomach and Upper Intestine, Tr. Am. Gastro-Enterol. A. (1930) **33**:81, 1931.

operations on gastric secretion are graphically illustrated in Figure 6 and in the table. The animal whose gastric secretion is charted in Figure 6 secreted an average of 14 mEq. of hydrochloric acid in each 24-hour period as a control Heidenhain pouch. The gastric secretion was increased 100%, to an average of 28 mEq. per day, when the duodenal contents were shunted into the gastric fundus. This amount represented an average of fifty 24-hour specimens. The gastric secretion increased markedly to an average of 72 mEq. per day when the duodenal content was shunted into the terminal ileum. This amount represented an average of sixty-nine 24-hour collections of gastric secretion.

Similar experiments were performed in three additional dogs. These secreted an average of 25 mEq. of hydrochloric acid in each 24-hour period. This amount

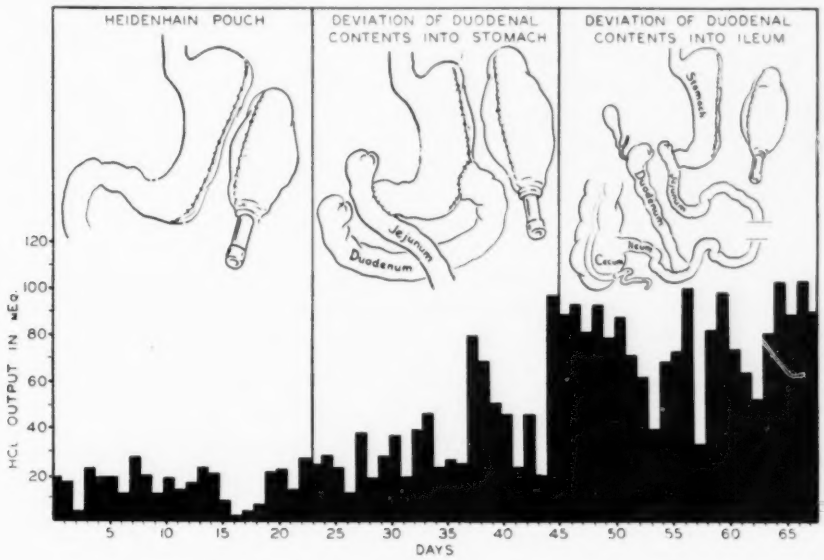

Fig. 6.—Effect of Mann-Williamson procedure on gastric secretion.

Gastric Secretion in Mann-Williamson Animals

Dog No.	Heidenhain Pouch	Duodenal Drainage to Stomach	Duodenal Drainage to Ileum
139	14 mEq.	28 mEq.	72 mEq.
143	31	38	87
150	31	76	81

represents an average of two hundred and fifty-two 24-hour collections of gastric juice from the Heidenhain pouch. When the alkaline duodenal contents were deviated into the stomach as in the McCann procedure, the average secretion from the Heidenhain pouches increased to 47 mEq. per day. This amount represents an average of one hundred and forty 24-hour collections. When the duodenal contents were then subsequently deviated into the lower ileum, as in the Mann-

Williamson procedure, the average secretion from the Heidenhain pouch increased to 80 mEq. per day, or more than three times the normal control level. This amount represents an average of one hundred and twenty-two separate 24-hour collections.

The cause of this profound augmentation in the output of acid from the stomach as a result of the Mann-Williamson procedure is not readily apparent. It has been often observed that animals operated on by this method sometimes have chronic diarrhea. Continued loss of the duodenal content in this manner could produce a systemic acidosis similar to that seen in animals provided with a permanent pancreatic fistula. Four Mann-Williamson animals (without accessory Heidenhain pouches) were prepared, and the carbon dioxide content, the pH, and the chlorides of the blood plasma were determined over a period of several weeks. These studies revealed that mild acidosis was usually present. The four animals, preoperatively, had an average pH of 7.52, a carbon dioxide content of 24.6 mM. per liter, and a chloride level of 108 mEq. per liter. After the duodenal deviation, the average pH was 7.32, the carbon dioxide content was 18.5 mM., and the chlorides 114 mEq.

The effect of systemic acidosis on gastric secretion was investigated in six dogs provided with accessory stomach pouches. After a control period of gastric juice collection, acidosis was produced by the oral administration of ammonium chloride or by the production of an external pancreatic fistula. In each case, the acidosis produced an increase in secretion from the isolated stomach pouch of 37, 130, 80, 51, 40, and 78% respectively. The average increase in secretion produced by the acidosis amounted to 69% above the control level. However, when blood chemistry studies were made on a series of Heidenhain pouch dogs in which the duodenal contents were deviated into the stomach, and then subsequently into the lower ileum, no alterations from the normal values were found. Apparently the loss of hydrochloric acid by way of the Heidenhain pouch produced sufficient alkalosis to offset the acidosis resulting from the Mann-Williamson procedure.

COMMENT

It is probable that the explanation offered by Exalto, and by Mann and Williamson, that the cause of marginal ulceration, which occurs after surgical internal duodenal drainage, is lack of neutralizing alkaline secretions at the gastrojejunal stoma is essentially correct. This view has been universally accepted. The data obtained in the present experiments, however, permit us to conclude that there is an additional cause, probably of equal importance, namely, the marked augmentation in the secretion of acid and pepsin by the stomach produced by this procedure. Simple hypersecretion of gastric juice produced by the implantation of pellets of histamine and beeswax into the subcutaneous tissues, as in the experiments of Hay, Varco, Code, and Wangensteen,[10] regularly leads to the production of typical progressive ulcers in a wide variety of experimental animals. Recently, Dragstedt, Oberhelman, and Smith[11] have demonstrated that a hypersecretion of gastric juice with ulcer formation can be regularly produced by the implantation of the antrum of the stomach into the colon as a diverticulum.

10. Hay, L. J.; Varco, R. L.; Code, C. F., and Wangensteen, O. H.: Experimental Production of Gastric and Duodenal Ulcers in Laboratory Animals by Intramuscular Injection of Histamine in Beeswax, Surg., Gynec. & Obst. **75**:170, 1942.

11. Dragstedt, L. R.; Oberhelman, H. A., Jr., and Smith, C. A.: Experimental Hyperfunction of the Gastric Antrum with Ulcer Formation, Ann. Surg., to be published.

The cause of the marked increase in gastric secretion in Mann-Williamson animals has not been determined. It is possible that systemic acidosis may be a factor in this stimulation, since we have observed that mild acidosis regularly occurs in Mann-Williamson dogs, and a comparable acidosis produced by the administration of ammonium chloride causes a significant increase in gastric secretion. Acidosis, however, is not the sole cause of the increase in gastric secretion which occurs in Mann-Williamson animals, since this acidosis was offset by the alkalosis resulting from the loss of gastric juice by way of the Heidenhain pouches, but nevertheless the increase in secretion of gastric juice was still observed. It is possible that absence of the usual inhibition of gastric secretion due to the presence of acid in the duodenum may be in part responsible for gastric hypersecretion in the Mann-Williamson preparations. It has been demonstrated by Pincus, Thomas, and Rehfus [12] that when the pH of the duodenal content is below 2.5, inhibition of gastric secretion results. By inspection of the drawings in Figure 6, it is clear that in the control pouch animal (Fig. 6*A*) acid from the stomach passes normally into the duodenum. When the duodenal content is deviated into the stomach, as in the experiment of McCann (Fig. 6*B*), some acid may still get into the duodenum by regurgitating backward from the stomach. However in the Mann-Williamson animal (Fig. 6*C*), it is clear that no acid can get into the duodenum, and thus no inhibition of gastric secretion from this source could occur.

CONCLUSIONS

1. The Mann-Williamson procedure produces a twofold to threefold augmentation in the output of hydrochloric acid by the stomach. Hypersecretion of gastric juice of this degree is sufficient to produce gastrojejunal ulceration; hence it may be concluded that the Exalto-Mann-Williamson ulcer is due not only to the absence of the neutralizing effect of the duodenal secretions at the stoma but also to a hypersecretion of acid gastric juice.

2. The cause of the increase in gastric secretion in Exalto-Mann-Williamson animals has not been determined.

12. Pincus, I. J.; Thomas, J. E., and Rehfuss, M. E.: A Study of Gastric Secretion as Influenced by Changes in Duodenal Acidity, Proc. Soc. Exper. Biol. & Med. **51**:367, 1942.

PULMONARY EMBOLISM FOLLOWING VENOUS LIGATION

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THE PURPOSE of this paper is to report an unusually high incidence of pulmonary embolism following venous ligation during the past year at Duke Hospital, where cases of thromboembolic disease on the surgical and gynecological services are referred to a consultant committee on thromboembolic diseases composed of the present authors.

A statistical analysis of all our cases over the preceding years is not intended in this report, since our series is similar in incidence and type of thromboembolism to those already reported in the vast amount of literature on this condition. However, during the 12-month period from July, 1950, to June, 1951, there were 50 patients with thromboembolic disease on the surgical (specialties included) and gynecological services. Of these, 43 were treated with anticoagulants only and 7 were primarily subjected to venous ligations, of whom 5 subsequently received anticoagulation therapy.

Of the seven patients who underwent venous ligation, pulmonary emboli developed after ligation in five. Four patients (Cases 1, 2, 3 and 4) underwent bilateral ligation of the superficial femoral veins just distal to the deep femoral branch. Of these, three (Cases 1, 2 and 3) had pulmonary emboli following ligation, with one death (Case 1); the other two were treated with anticoagulants and recovered. Two patients (Cases 5 and 6) were subjected to bilateral ligation of the common femoral and saphenous veins. One of these had an uneventful course, and the other (Case 5) had a pulmonary embolus after the ligation, was treated with anticoagulants and recovered; he has been maintained on bishydroxycoumarin (dicumarol®) on an outpatient basis in view of a marked clotting tendency mainly of the veins distal to the points of ligation and also because of a mild type of migratory phlebitis of the arm veins.

One patient (Case 7) underwent bilateral popliteal ligation for deep venous insufficiency, as advocated by de Takats and Graupner,[1] and had a pulmonary embolus after the ligation; he was treated with anticoagulants and recovered. (See table.)

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1. de Takats, G., and Graupner, G. W.: Division of the Popliteal Vein in Deep Venous Insufficiency of the Lower Extremities, Surgery **29**:342-354, 1951.

REPORT OF CASES

CASE 1 (W. J. S.).—A 74-year-old Negro was admitted to the hospital on Oct. 31, 1950, with benign prostatic hypertrophy and a large bladder stone.

On November 3, while he was under spinal anesthesia supplemented by thiamytal sodium (surital®) and nitrous oxide, suprapubic cystolithotomy and bilateral vasectomy were performed. On November 10, a transurethral prostatic resection was performed, the same anesthesia being used. On November 12, two days after the prostatic resection, he complained of severe right chest pain. A roentgenogram of the chest (the roentgenogram made on his admission had been negative) was compatible with the diagnosis of a pulmonary infarction of a segment of the right lower lobe. The patient had no signs of peripheral thrombosis, and the impression was that he had phlebothrombosis of the pelvic veins with pulmonary embolism. He was given heparin therapy, but in view of the recurrence of urethral bleeding and the subsidence of his symptoms, this was discontinued on November 16. He did well until November 20, when marked signs of thrombophlebitis of both legs developed; on that day, with the use of local procaine anesthesia, a bilateral ligation of the superficial femoral veins was performed. At the time of this operation blood clots were noted in the vein proximal to the point of ligation, and these were removed by suction. On November 22, after doing well for two days, he was seized with sudden severe chest pain while on a bed pan, and he died within a period of 10 minutes, presumably of a massive pulmonary embolus. Permission for autopsy was not granted.

Patients with Bilateral Venous Ligations

Case	Site of Ligation, Vein	Pulmonary Embolus			Result
		Before Ligation	After Ligation	No. of Days After Ligation	
1	Superficial femoral	Yes	Yes	2 days	Died
2	Superficial femoral	No	Yes	11 days	Recovered
3	Superficial femoral	No	Yes	4 days	Recovered
4	Superficial femoral	No	No	None	Recovered
5	Common femoral and saphenous	Yes	Yes	15 days	Recovered
6	Common femoral and saphenous	No	No	None	Recovered
7	Popliteal	No	Yes	2 days	Recovered

Summary.—A 74-year-old Negro had the signs of a pulmonary embolus to the right lung on the second day after a transurethral resection. Heparinization was followed by bleeding from the urethra; heparin therapy was discontinued prematurely, and thrombophlebitis of both legs developed. Bilateral ligation of the superficial femoral veins was carried out, with blood clots noted in the proximal veins. These were removed by suction. Two days after the ligation, severe chest pain developed and the patient died within a period of 10 minutes. Permission for autopsy was not granted.

CASE 2 (A. S. P.).—A 62-year-old white man was admitted to the hospital on Feb. 13, 1951, with a preoperative diagnosis of carcinoma of the stomach and bilateral thrombophlebitis of the lower extremities. In view of an imminent exploratory laparotomy for carcinoma, he underwent bilateral ligation of the superficial femoral veins while under local procaine anesthesia. Two days later an exploratory laparotomy was performed, general anesthesia being used, and an irremovable carcinoma of the stomach was encountered, with extensive metastases to the liver and the peritoneum. No palliative procedure was done. The postoperative course was uneventful until the ninth day, at which time he complained of some pain in the right lateral lower region of the chest; during the ensuing days a diagnosis of pulmonary embolism was confirmed by x-ray changes at the right base compatible with infarction (roentgenogram of the chest on his admission was negative), bloody sputum, and a friction rub over the same aren. After an eight-day course of anticoagulation, he was discharged in good condition.

Summary.—A 62-year-old white man with irremovable carcinoma of the stomach underwent bilateral ligation of the superficial femoral veins prior to laparotomy for bilateral thrombophlebitis. On the ninth day after laparotomy a typical pulmonary embolus to the right lung base developed, and after an eight-day course of anticoagulation he was discharged in good condition.

CASE 3 (T. H. R.).—A 77-year-old white man was admitted to the hospital on June 17, 1951, with benign prostatic hypertrophy. On June 20, 1951, a bilateral vasectomy and transurethral prostatic resection was performed with the patient under spinal anesthesia. He had had thrombophlebitis of the right leg 12 years before his admission, and on the second postoperative day ankle edema developed, along with tenderness of the right calf and a positive Homans sign.

In view of the previous experience with bleeding after heparin therapy in two other patients with thrombophlebitis following transurethral resections and the localization of symptoms and signs to the distal half of the right lower extremity, bilateral ligation of the superficial femoral veins was carried out. At the time of operation no blood clots were evident at the site of ligation just distal to the deep femoral branch on either side.

Four days after the venous ligations on June 26, 1951, the patient complained of right chest pain laterally without other physical signs. A roentgenogram of the chest (negative on admission) revealed a density at the right base compatible with a pulmonary infarction. He had no further embolic episodes and was discharged on the 15th postoperative day in good condition.

Summary.—A 77-year-old white man suffered from thrombophlebitis of the right lower leg two days after a transurethral resection. Bilateral ligation of the superficial femoral veins was performed, and two days later he had a pulmonary embolus to the right lung laterally.

CASE 4 (R. E. H.).—A 38-year-old Negro was admitted to the hospital on May 31, 1951, with intestinal obstruction eight months after a ruptured appendix with generalized peritonitis. The patient was markedly dehydrated, with moderate electrolyte imbalance. He was treated conservatively with a Cantor tube and intravenous alimentation. On June 5, thrombophlebitis of the deep venous system of both legs developed, and in view of an impending laparotomy, bilateral ligation of the superficial femoral veins was performed with the patient under local anesthesia. No clot was noted at the points of ligation just distal to the deep femoral branch. On June 20, after several episodes of temporary improvement and exacerbation of the gastrointestinal symptoms, an exploratory laparotomy was performed and an inflammatory and stenotic portion of the ileum resected. The postoperative course was uncomplicated, and there were no embolic phenomena.

Summary.—A 38-year-old Negro with intestinal obstruction had bilateral thrombophlebitis of the deep veins of both lower extremities prior to laparotomy. He underwent bilateral ligation of the superficial femoral veins, without any embolic complications.

CASE 5 (E. L. F.).—A 48-year-old white man was seen in February, 1950, at which time he was found to have a duodenal ulcer; he has been maintained on banthine therapy since then.

In January, 1951, he began to experience transient episodes of a migratory type of pain involving both thighs, and sometimes both calves and later the dorsum of his left foot.

On May 27, 1951, he was admitted to the hospital six hours after the sudden onset of pain in the left lower region of the chest. His family physician had been treating him with dicumarol* for the four weeks prior to his admission, but his prothrombin level was 100% on admission. The treatment had been instituted by the family physician after the diagnosis of recurrent episodes of thrombophlebitis bilaterally. At the time of his admission a roentgenogram of the chest revealed haziness of the left anterior lower lobe, and he was subjected to a bilateral ligation of the common femoral and saphenous veins. The pathological report of the segments of vein removed revealed organizing and recanalizing thrombi of the femoral veins bilaterally. The patient's postoperative course was uneventful, and he was discharged on the 14th postoperative day.

The day after his discharge, on June 11, 1951, he was readmitted because of chest pain on the opposite (right) side, with blood-tinged sputum and shortness of breath. A roentgenogram of the chest revealed a lesion at the right base compatible with a second pulmonary infarct. He was immediately given anticoagulant therapy with heparin and bishydroxycoumarin (dicumarol*) and discharged on the 15th hospital day on bishydroxycoumarin therapy (which has been kept up on an outpatient basis) without new episodes of pulmonary infarction clinically or roentgenologically. Follow-up roentgenograms of the chest suggest an area of necrosis in the right lung base. He has continued to have edema of both legs, especially the left, and transient episodes of migratory phlebitis of both the long saphenous veins and the right antecubital arm veins. However, he has had no further emboli.

Summary.—A 48-year-old white man on banthine® (beta-diethylaminoethyl xanthene-9-carboxylate-methobromide) therapy for a duodenal ulcer had a migratory type of phlebitis of his lower extremities, and a pulmonary infarction of the left lower lobe developed. He underwent bilateral ligation of the common femoral and saphenous veins, and 15 days later he had a pulmonary embolus to his right lower lobe. He was subsequently treated with anticoagulants and has been maintained on bishydroxycoumarin on an outpatient basis.

CASE 6 (G. C. W.).—A 68-year-old white man was admitted to the hospital on April 16, 1951, and underwent a combined abdominal-perineal resection for an adenoma malignum. On April 28, on the eighth postoperative day, thrombophlebitis of the deep veins of both lower extremities developed and he was given anticoagulant therapy. However, on May 5, because of acute urinary retention due to benign prostatic hypertrophy, administration of bishydroxycoumarin was stopped on the seventh day of anticoagulation, and on May 7 a bilateral ligation of the common femoral and superficial saphenous veins was done and followed immediately by a transurethral prostatic resection. The patient's postoperative course was uneventful and uncomplicated by embolic phenomena.

Summary.—A 68-year-old white man had bilateral thrombophlebitis after a combined abdominal-perineal resection. He was treated with anticoagulants, but this therapy was discontinued on the seventh day because of acute urinary retention due to benign prostatic hypertrophy. A bilateral ligation of the common femoral and saphenous veins and a transurethral prostatic resection were done, with no postoperative embolic complications.

CASE 7 (W. O. T.).—A 61-year-old white man was admitted to the hospital on Nov. 21, 1950, with bilateral varicose veins, bilateral chronic stasis ulcers of 15 years' duration, and a recurrent left inguinal hernia. On the fourth hospital day after a period of conservative treatment of the stasis ulcers, a McVay type of repair of the hernia was done, and four days later a bilateral ligation of the popliteal veins was performed for the ulcers. Two days after the venous ligation sudden severe pain developed in the left chest; an electrocardiogram was negative, and a portable chest roentgenogram revealed changes in both lower lobes compatible with pulmonary emboli. He was immediately given anticoagulant therapy. The following day he had some blood-streaked sputum and a friction rub was heard over the left lower lobe posterolaterally. Anticoagulation was continued for 12 days, and he was discharged shortly thereafter with jelly-boots on both lower extremities.

Summary.—A 61-year-old white man had pulmonary emboli two days after bilateral popliteal vein ligation for stasis ulcers. He was discharged after a 12-day course of anticoagulation.

COMMENT

It is generally understood that thrombophlebitis of the lower extremities is merely a local manifestation of a generalized thrombotic disease. The only rationale in the past for superficial femoral vein ligation has been the belief that the major source of emboli emanated from sites distal to the point of ligation.

In 1948, Crutcher and Daniel [2] correlated the clinical and autopsy findings in pulmonary embolism. In 23 of the 55 cases of fatal pulmonary embolism reviewed by them, the thrombi were found in the veins of the pelvis and the upper abdomen. They concluded that in those 23 cases ligation of the femoral veins could not have prevented pulmonary embolism but that ligation of the inferior vena cava might have done so.

In 1949, Allen [3] reported that in a group of 1,500 patients who underwent therapeutic interruption of the superficial femoral veins for thrombophlebitis there

2. Crutcher, R. R., and Daniel, R. A., Jr.: Pulmonary Embolism: A Correlation of Clinical and Autopsy Studies, Surgery **23**:47-62, 1948.

3. Allen, A. W.: The Present Evaluation of the Prophylaxis and Treatment of Venous Thrombosis and Pulmonary Embolism, Surgery **26**:1-7, 1949.

were seven cases of fatal pulmonary emboli following ligation; similarly, in a group of 1,078 patients with prophylactic bilateral superficial femoral ligations there were five cases of fatal pulmonary emboli. In their five-year report on thromboembolic disease, in 1951, Ravdin and Kirby [4] describe three patients with phlebothrombosis who had pulmonary infarctions following superficial femoral vein ligation but recovered on heparinization; one patient given heparin therapy had repeated infarcts which stopped after ligation. They also reported two cases of embolism which occurred after prophylactic ligation of the superficial femoral veins.

Recently, McLachlin and Paterson [5] in an excellent study have reported their findings in routine autopsies on 100 unselected male patients over the age of 40 years; they gave special attention to the lungs and to the veins of the lower extremities. In 34% of the cases there were grossly demonstrable venous thrombi and in 56% of these cases (19% of the total series) there was a pulmonary embolus. Seventy-three per cent of the thrombi arose in the thigh and pelvic veins proximal to the usual point of ligation of the superficial femoral veins. They concluded that surgical ligation of the superficial femoral veins either prophylactically or therapeutically in pulmonary embolism did not appear basically sound.

Also recently, Erb and Schumann [6] have reported an interesting study of 100 consecutive cases of fractures of the femoral neck. In alternate cases bilateral ligation of the superficial femoral veins had been performed prophylactically; there was no difference in the incidence of pulmonary embolism between the group of 50 patients who underwent ligation and the control group of 50 patients. Among the patients examined at autopsy, the only case of pure fatal pulmonary embolism was in the ligated group; also the incidence of nonfatal pulmonary embolism was higher in the ligated group. They concluded that in aged patients with fractures of the neck of the femur bilateral superficial femoral vein ligation did not lower the mortality due to pulmonary embolism nor the incidence of nonfatal pulmonary emboli; they also concluded that ligation in such patients was frequently followed by thrombosis, arising in the proximal femoral vein compartment, and that pulmonary embolism was a common concurrence.

In our cases, five of seven patients with venous ligation had pulmonary emboli 2 to 15 days after ligation. In the 43 others in the same year who were treated with anticoagulants, no pulmonary emboli were noted during the period of active therapy or after the discontinuance of anticoagulation; there were no instances of severe hemorrhage due to the use of anticoagulants.

The following are some of the conditions commonly listed in the literature as contraindications for anticoagulation and indications for venous ligation: thrombophlebitis occurring (*a*) preoperatively or ante partum, (*b*) after operation on the brain and spinal cord, (*c*) after operations in which large denuded surfaces are left, e. g., abdominoperineal resections of the rectum, or (*d*) in patients with hepatic or renal insufficiency. Jaimet [7] has reported on 16 surgical patients and 90 obstetrical

4. Ravdin, I. S., and Kirby, C. K.: Experiences with Ligation and Heparin in Thromboembolic Disease, Surgery **29**:334-341, 1951.

5. McLachlin, J., and Paterson, J. C.: Some Basic Observations on Venous Thrombosis and Pulmonary Embolism, Surg., Gynec. & Obst. **93**:1-2, 1951.

6. Erb, W. H., and Schumann, F.: An Appraisal of Bilateral Superficial Femoral Vein Ligation in Preventing Pulmonary Embolism, Surgery **29**:819-825, 1951.

7. Jaimet, C. H.: Anticoagulant Therapy, Canad. M. A. J. **61**:10-13, 1949.

patients who were being treated with bishydroxycoumarin at the time of operation and delivery, respectively; the prothrombin times ranged between 30 and 40 seconds, and no instances of abnormal bleeding were encountered. Also in Case 2 (see above) preoperative ligation of the superficial femoral veins for thrombophlebitis did not prevent the patient from having a pulmonary embolus after an exploratory laparotomy. It is our suggestion that patients with preoperative thrombophlebitis be treated with heparin only for at least 48 hours prior to elective surgery; at the scheduled time of operation the heparinization can be reversed within 15 minutes by the intravenous administration of protamine sulfate (usual dose, 50 mg.) and can be reinstituted 6 to 12 hours after the conclusion of the operative procedure. At that time bishydroxycoumarin can be given simultaneously. In our experience patients in whom thrombophlebitis developed after operations on the brain and spinal cord have had no complications from anticoagulant therapy; the same has been true for patients in whom thrombophlebitis developed after abdominoperineal resections. Patients with hepatic or renal insufficiency in whom thrombophlebitis develops can be treated with small doses of heparin only; in this group of patients the use of bishydroxycoumarin should be avoided.

To date, the only contraindication for anticoagulation therapy that we have encountered in surgical cases is in patients undergoing postoperative transurethral prostatic resection who bleed readily on heparinization, presumably due to the washing action of the urinary stream. The bleeding stops when heparinization is reversed with protamine sulfate; yet in this group two patients had pulmonary emboli after superficial femoral vein ligation, and one died. This situation has stimulated the Urology Service into repeating the work of Kay and others [8] and determining antithrombin titers preoperatively and postoperatively in patients undergoing transurethral prostatic resection, before and after alpha-tocopherol and calcium gluconate therapy. The results [9] do not appear to corroborate the findings of Kay and others [8] and will be published separately.

At the present time the only plausible way of preventing fatal pulmonary emboli and avoiding serious hemorrhage in patients who have undergone transurethral resection and in whom thromboembolic disease develops appears to be by the performance of inferior vena cava ligation. Collins and others [10] have recently pointed out the necessity for inferior vena cava ligation in suppurative pelvic thrombophlebitis in women; perhaps the prostate deserves the same respect in the male. Another indication for inferior vena cava ligation to consider is pulmonary embolism despite adequate heparinization; for us, the term "adequate heparinization" implies a prolongation of the clotting time to 30 minutes or more; no such case of embolism has occurred in our series, but one instance of it was reported by Ravdin and Kirby.[4]

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8. Kay, J. H.; Hutton, S. B., Jr.; Weiss, G. N., and Ochsner, A.: Studies on an Antithrombin: III. A Plasma Antithrombin Test for the Prediction of Intravascular Clotting. Surgery **28**:24-28, 1950.

9. Boone, A. W.: Personal communication to the authors.

10. Collins, G. D.; MacCallum, E. A.; Nelson, E. W.; Weinstein, B. B., and Collins, J. H.: Suppurative Pelvic Thrombophlebitis: I. Incidence, Pathology and Etiology. Surgery **30**:298-310, 1951.

Except for the indications of inferior vena cava ligation as discussed above, it is questionable whether or not there is any indication for ligation of the superficial femoral or the common femoral veins in thromboembolic disease. Case 3 appeared to be an ideal case for superficial femoral vein ligation, since the symptoms were localized to the right calf only and at operation no clot was apparent in either superficial femoral vein; yet four days after ligation the patient had a pulmonary embolus. A final argument against femoral ligation is that to ligate a phlebitic vein at its proximal end when it is already to be taxed by incompetent valves and areas of recanalization appears to add insult to injury. We have observed that patients who receive anticoagulation therapy have considerably fewer postphlebitic complications than patients undergoing vein ligation; most remarkable has been the absence of pain, edema, ulceration, and recurrent episodes of phlebitis caused by stasis distal to the point of ligation. The interesting studies of DeCamp and his collaborators [11] have revealed a sharp increase in the ambulatory venous hypertension of two patients with the postphlebitic syndrome subjected to superficial femoral or popliteal vein ligation.

It is an erroneous impression that adequate anticoagulation therapy can be effected only in major university centers or large hospitals, and surgeons in smaller hospitals have been encouraged in the past to perform ligation of the superficial femoral veins. Certainly bishydroxycoumarin should not be administered where facilities to determine prothrombin levels are not available. However, there should be no contraindication to administering heparin in a repository form (average dose, 400 mg.) once a day intramuscularly. The modified three-tube Lee-White method of determining clotting time is a procedure requiring no special equipment or facilities and is an adequate method for evaluating heparin therapy when performed two to three times per day.[12] There is no justification for a feeling of security from fatal pulmonary embolism following ligation of the superficial femoral or common femoral veins.

SUMMARY AND CONCLUSIONS

During the past year, five of seven patients undergoing venous ligations for thromboembolic disease had pulmonary emboli between 2 to 15 days after ligation, with one fatality. Forty-three other patients with thromboembolic disease during the same year who were treated with anticoagulants did not have any pulmonary emboli during active therapy or after discontinuance of anticoagulation.

Some of the reports of pulmonary embolism following ligation of the superficial femoral veins have been reviewed. It is proposed that patients in whom pulmonary emboli develop after transurethral prostatic resections be subjected to inferior vena cava ligation. Indications for inferior vena cava ligation are discussed. A discussion of the rationale for superficial and common femoral vein ligation is submitted. It

11. DeCamp, P. T.; Schramel, R. J.; Ray, C. J.; Feibleman, N. D.; Ward, J. A., and Ochsner, A.: Ambulatory Venous Pressure Determinations in Post-Phlebitic and Related Syndromes, Surgery **29**:44-70, 1951.

12. Duff, Linman, and Birch (The Administration of Heparin, Surg., Gynec. & Obst. **93**:343-362, 1951) have recently published a comprehensive review on the administration of heparin to which the reader is referred for details of heparinization; their experience appears to be similar to ours.

is concluded that there is no justification for a feeling of security from fatal pulmonary embolism following ligation of the superficial femoral or common femoral veins.

Anticoagulation therapy appears to be the treatment of choice; when facilities for prothrombin determinations are not available, it is suggested that heparin in repository form given once a day intramuscularly be used in preference to ligation of the superficial femoral veins.

NOTE—E. L. F. (Case 5) has been found to have an underlying bronchogenic carcinoma of the left lower lobe; this finding does not alter the fact that he had a pulmonary embolus to the right lung following ligation which x-ray examination now shows to have cleared completely.

CYSTS OF THE PARATHYROID

Report of Three Cases Clinically Simulating Nodular Goiter

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AND
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THE OCCURRENCE of three lateral cysts of the neck apparently arising from parathyroid tissue led us to review the literature on this subject. While microscopic cystic areas in the parathyroid are common [1] and small macroscopic cysts discovered at autopsy are occasional,[2] large cysts presenting as swellings in the side of the neck are rare. Only eight such cases were found in the literature,[3] although others have alluded to instances of large parathyroid cysts. Lahey [4] states: "We have operated upon a few patients for local tumors of the neck in whom the diagnosis was not certain but in whom the pathological report following removal has been a cyst arising in a non-hyperfunctioning parathyroid adenoma."

As the parathyroids arise from the branchial clefts, it is perhaps unwarranted to separate lateral cervical cysts with parathyroid tissue in their walls from other cysts of branchial origin. The distinguishing features seem to be (1) the occurrence of fields of typical parathyroid cells in the cyst wall, (2) a cyst lining of cuboidal or columnar epithelium, and (3) the location of the cysts in a position corresponding to that of the parathyroid glands.

The first report of a large parathyroid cyst was published by Goris [3a] in 1905. The patient, a 22-year-old man, had noted a mass in his neck for three years which clinically was described as a lobulated tumor with the consistency of a ganglion. At

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Surgical Clinic and the Department of Surgical Pathology of the Hospital of the University of Pennsylvania.

1. Sandström, I.: Om en ny körtel hos människan och åtskilliga däggdjur, Upsala läkaref. förh. **15**:441-471, 1880.

2. (*a*) Peterson, H.: Anatomische Studie über die Glandulae parathyreoidae des Menschen, Virchows Arch. f. path. Anat. **174**:413-434, 1903. (*b*) von Verebley, T.: Beiträge zur Pathologie der branchialen Epithelkörperchen, ibid. **187**:80-105, 1907. (*c*) Thompson, R. L., and Harris, D. L.: Study of Parathyroid Gland from 250 Routine Autopsies at St. Louis City Hospital, J. Med. Res. **19**:135, 1908.

3. (*a*) Goris, D.: Extirpation de trois lobulus parathyroidiens kystiques, J. de chir. et ann. Soc. de chir. **13**:294-395, 1905. (*b*) Nylander, P. E.: Parathyroid Cyst of Neck: Case, Acta chir. scandinav. **64**:539-547, 1929. (*c*) McKnight, R. B.: Parathyroid Cyst, South. Surgeon **12**:179-184, 1946. (*d*) Welti, H.: Parathyroid Cysts: Cases, Mém. Acad. de chir. **72**:33-35, 1946.

4. Lahey, F. H.: Parathyroid Tumors, S. Clin. North America **27**:477-485, 1947.

operation it was found to consist of three adjacent cysts independent of the thyroid gland. Microscopically the cysts were composed of encapsulated colloid and degenerated parathyroid tissue.

In 1928, Nylander [3b] reported a goose-egg-sized cyst arising in the neck of a 16-year-old boy and clinically simulating a branchial cyst. The cyst wall was lined with columnar epithelium and contained much muscle and some parathyroid tissue. Nylander believed that the cyst took origin from the parathyroid tissue and represented a special type of lateral congenital cyst of the neck. A similar case involving a 17-year-old boy was reported by McKnight [3c] in 1946. The patient had been aware of a lump in the left side of the neck for some time and for two months before admission complained of hoarseness. On physical examination, a hard, golf-ball-sized tumor was palpable in the region of the left lower pole of the thyroid gland. It was slightly movable and displaced the trachea to the right. At operation the cyst showed no connection with the thyroid gland. The cyst contained a pale milky fluid. Although no epithelial lining was identified, parathyroid tissue was included in the cyst wall, and therefore McKnight assumed that the cyst originated from a parathyroid body.

Five additional cases were reported by Welti [3d] in 1946. He referred briefly to a case reported elsewhere in 1932 and reviewed four other cases in detail. His patients ranged from 35 to 53 years in age, and all were women. They all noted a swelling in the neck. One patient, whose mass is described clinically as the size of an orange, complained of difficulty in swallowing and breathing. Examination of the vocal cords showed recurrent nerve paralysis on the side of the lesion in two instances, and at operation the recurrent nerve was intimately adherent to the lesion. Welti commented on the impossibility of clinical diagnosis, since these cysts simulated goiter clinically and moved on swallowing. In his five cases, all cysts were found at operation to be below and behind the inferior pole of the thyroid, although entirely independent of the thyroid gland. In two of his cases, the lower pole of the cyst extended into the thorax. Welti identified these cysts as parathyroid cysts because (1) the location of the cysts corresponded to that of the inferior parathyroids, (2) parathyroid tissue was usually present histologically, and (3) the lining of the cyst was cuboidal epithelium, when identifiable.

REPORT OF CASES

CASE 1.—In October, 1945, a 39-year-old white woman was admitted to the Hospital of the University of Pennsylvania with a slowly enlarging swelling in the lower anterior portion of her neck present for the preceding two and one-half years. There were no symptoms of thyroid toxicity, and the basal metabolic rate was —13. Physical examination revealed no abnormalities except for a soft indefinite swelling anteriorly in the lower portion of the left side of the neck. At operation a large cyst measuring 7 by 3 cm., independent of the thyroid gland and extending into the mediastinum, was found and removed.

Microscopically, the cyst wall was thin and composed of vascular fibrous tissue. It was lined with a single layer of cuboidal or low columnar cells with sharp borders, pale or clear cytoplasm, and small, very dark, round nuclei, usually situated basally. Parathyroid tissue was seen in the cyst wall. The cells lining the cyst closely resembled the parathyroid cells (Fig. 1).

CASE 2.—The second patient, a 33-year-old woman, was admitted to the hospital in May, 1949, because of a progressive swelling in her neck present for eight months. Otherwise, she was asymptomatic. A soft mass was palpable in the right side of the neck, extending across the midline and moving on swallowing. Mirror laryngoscopy showed normal movement of the vocal cords. Preoperative values for serum calcium, phosphorus, and alkaline phosphatase were

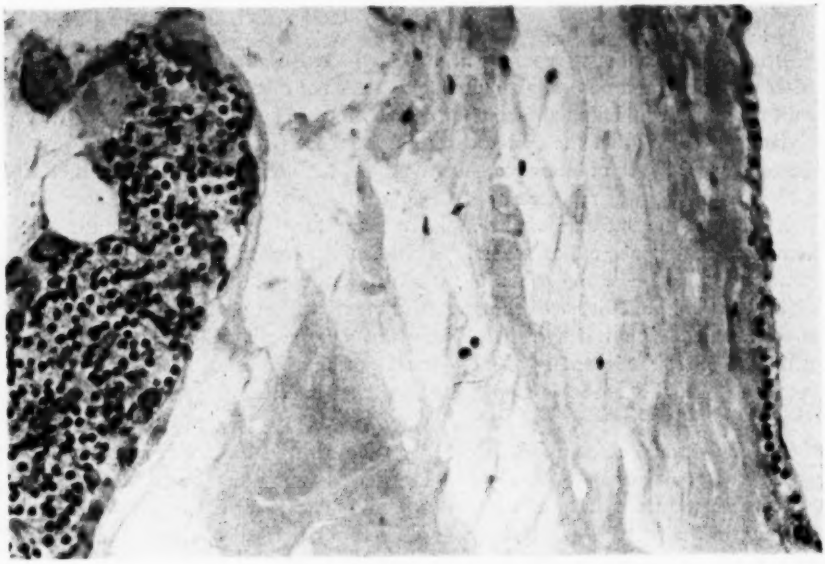

Fig. 1 (Case 1).—The cyst is lined by a single layer of cuboidal epithelial cells, and parathyroid tissue is present in the wall; ×240.

Fig. 2 (Case 2).—Gross appearance of the cyst.

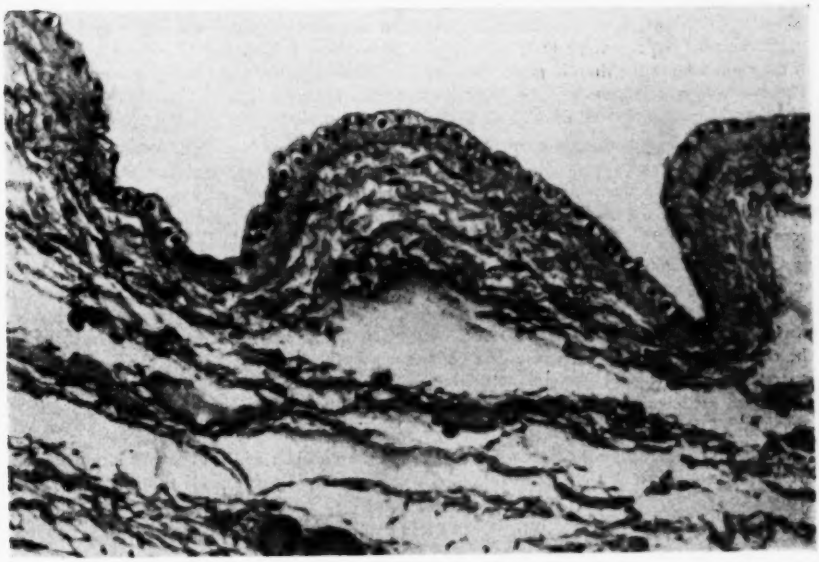

Fig. 3 (Case 2).—Single layer of cuboidal epithelium lining the cyst; × 240

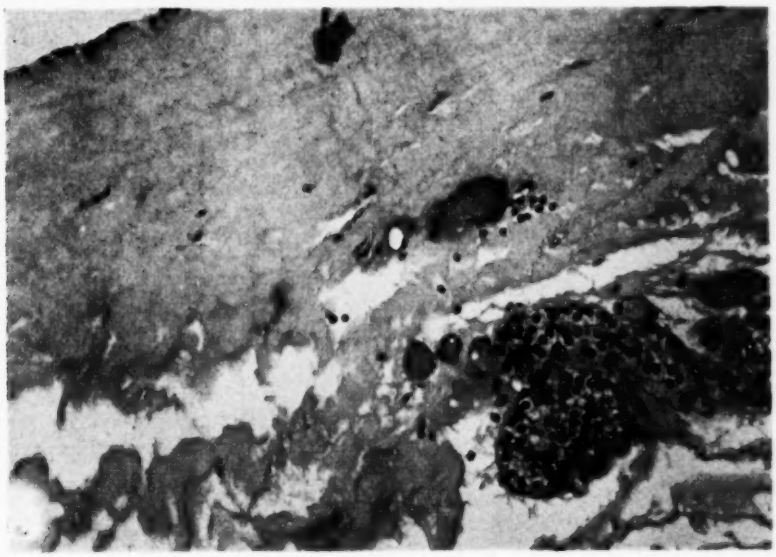

Fig. 4 (Case 3).—Parathyroid tissue is identified in the cyst wall; × 240.

not obtained, but postoperatively the serum calcium level was 10.7 mg. per 100 cc., phosphorus 3.4 mg., and alkaline phosphatase 2.5 Shinowara units. The basal metabolic rate was +15. At operation there was found a membranous, lobulated monolocular cyst measuring 9 by 4 by 3 cm. and containing clear, watery fluid (Fig. 2). It arose from behind and below the inferior pole of the right lobe of the thyroid gland, pushing the latter cephalad, and readily separable from it. The cyst was largely subclavicular, with a tongue-like extension into the superior mediastinum. The thyroid gland appeared normal.

Microscopic examination showed the cyst to be lined with a single continuous layer of cuboidal cells with oval vesicular nuclei (Fig. 3). No parathyroid tissue was seen in the cyst wall. However, the location of the cyst, its clear, watery content, easy separability from the thyroid gland, and the similarity of the lining epithelium to that in Case 1, suggested its origin from parathyroid.

CASE 3.—The third patient, a 29-year-old woman, first noted a small lump in the lower anterior portion of the right side of the neck six weeks prior to her admission to the hospital in November, 1950. She had no other symptoms. On physical examination a firm, resilient, marble-sized nodule which moved on swallowing was noted in the region of the lower pole of the right lobe of the thyroid gland. At operation a cyst measuring 1.2 by 1.0 by 0.9 cm. was separated through a good cleavage plane from the lower pole of the right thyroid lobe. Exploration of the left lobe of the thyroid and the remainder of the right lobe showed no abnormality.

On microscopic examination, the cyst wall was found to consist of a dense hyaline fibrous tissue in which a few lymphocytes were noted. Simple cuboidal epithelium with clear colorless cytoplasm lined much of the cyst. Parts of the wall contained parathyroid tissue (Fig. 4).

COMMENT

The three cysts described, bringing the total number of reported cases to 11, appear to meet the diagnostic criteria of parathyroid cysts. Two occupied the position of the right lower parathyroid gland and one that of the left lower parathyroid gland. All were lined by cuboidal or low columnar epithelial cells resembling those of the parathyroid. Parathyroid tissue was identified in the walls of two of the cysts.

What is the origin of these large cysts? Thompson and Harris [2c] classified cysts occurring in connection with the parathyroid glands as follows:

1. Simple retention cysts which are filled with colloid.
2. Polycystic degeneration with a coalescence of small cysts.
3. Congenital cysts arising in and around the parathyroid glands, developmental anomalies of the gill pouches, as are the branchial cysts.

Small retention type cysts of the parathyroid glands are not uncommon and are found in 2 to 12% of persons in routine autopsies.[3] Thompson and Harris [2c] state that such cysts may be single or multiple but they rarely exceed the diameter of a low-power field. Cysts of the parathyroid arising as a result of polycystic degeneration within the gland with a coalescence of such small cysts are thought to be exceedingly rare.[2c]

Those parathyroid cysts thought to be congenital are considered developmental anomalies of the gill pouches. The superior parathyroids embryologically develop from the fourth gill pouches and the inferior parathyroids from the third gill pouches. Branchial cysts might then occur within, or closely associated with, the parathyroid bodies.

Welti [3d] concluded that large cysts in which parathyroid tissue was included within the cyst wall probably represented cystic development in the adult parathyroid gland but that in instances in which the parathyroid tissue was independent of the cyst wall the cysts were probably of branchial origin.

Since the origin of these cysts is uncertain, it would seem best to classify them as a special type of lateral cyst of the neck, possibly congenital, arising in connection with the parathyroid glands.

SUMMARY

Three cases of lateral cysts of the neck apparently arising from parathyroid tissue are presented. Only eight additional such cases were found in a survey of the literature. These cysts are independent of the thyroid gland and are not hyperfunctioning. The presenting symptom is a swelling in the anterior portion of the neck. There was evidence of recurrent nerve involvement on the side of the lesion in three of the patients previously reported. Four of the 11 cysts were found to extend into the mediastinum.

INTRAVENOUS SODIUM 5-ALLYL-5-(1-METHYLBUTYL) BARBITURATE FOR HYPNOSIS DURING NITROUS OXIDE ANESTHESIA

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MANY members of the barbituric acid series have been investigated with reference to their use as hypnotics in anesthesia. Fitch, Waters, and Tatum [1] in their extensive work on barbituric acid derivatives emphasized the importance of short-acting members in anesthesiology.

Sodium 5-allyl-5-(1-methylbutyl) barbiturate (secobarbital [seconal®] sodium) appeared to be a desirable compound for use in anesthesiology.

Swanson [2] reported its use in dogs. He showed that seconal® sodium produced hypnosis slightly more intense than that obtained with pentobarbital sodium and comparable to that obtained with amobarbital (amytal®) sodium. The time for complete recovery with seconal,® however, was one-half that with amytal® and slightly less than that with pentobarbital sodium.

Barlow and his co-workers [3] reported that tolerance did not develop in dogs receiving repeated intravenous administration of seconal® sodium. The drug did not appear to be excreted in the urine. Like all other members of the same group, seconal® sodium frequently caused lowering of blood pressure and depression of respiration in a few dogs when given intravenously at a rapid rate.

It was thus thought advisable to undertake further clinical investigation of seconal® sodium in anesthesiology. This work was started at Indiana University Hospitals in June, 1948.

Many investigators in recent years have advocated heavy barbiturate premedication prior to nitrous oxide anesthesia. Although thiopental (pentothal®) sodium is an excellent drug when combined with nitrous oxide during short procedures, it has been our experience that the drug has a cumulative action when given over long periods. It was felt that seconal® sodium given intravenously just prior to nitrous oxide anesthesia would eliminate the use of pentothal® or, at least, reduce the amount of the drug required during operation. The seconal® sodium used in the first part of the investigation was prepared in 5 cc. ampuls

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From the Department of Anesthesiology, Indiana University Hospitals.

Seconal® sodium was supplied through the courtesy of Eli Lilly & Company research laboratories.

Read before the Section on Anesthesiology at the One Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

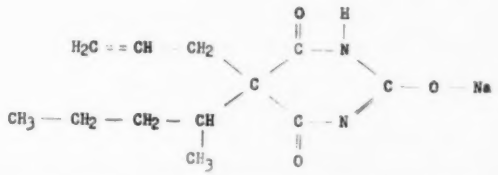
1. Fitch, R. H.; Waters, R. M., and Tatum, A. L.: Am. J. Surg. **9**:110, 1930.

2. Swanson, E. E.: Proc. Soc. Exper. Biol. & Med. **32**:1563, 1935.

3. Stermont, M. F.; Lampe, I., and Barlow, O. W.: J. Pharmacol. & Exper. Therap. **39**:165, 1930.

containing 250 mg. of salt dissolved in a 50% sucrose solution. This vehicle was used to give the preparation stability. Aqueous or alcoholic solutions tended to break down during storage.[4]

The above preparation was discarded after adequate clinical trial because of technical difficulties and complications encountered in administration. The preparation was difficult to remove from the ampul because of viscosity and many patients complained of pain and severe burning when the drug was injected intravenously even after dilution. In a few patients thrombophlebitis developed postoperatively which was attributed to the sucrose preparation of the drug. A preparation is now being used containing 250 mg. of seconal® sodium in 5 cc. of a polyethylene glycol and water vehicle. It has not been necessary to dilute this preparation, and none of the patients have complained of pain following intravenous injection. There have been no cases of thrombophlebitis attributable to this preparation.



Formula for secobarbital sodium (seconal® sodium, Eli Lilly & Company).

PRESENT STUDY

Two thousand five hundred patients were observed in the present study. The average age of the group was 41.2 years, with a range of 10 to 96 years. The average anesthesia time was 121 minutes. Selection of patients was made only with reference to ordinary precautions taken in the use of any barbiturate. Persons with congestive heart failure or orthopnea were not given this drug.

The premedication varied between morphine sulfate, 8 to 15 mg., and scopolamine hydrobromide or atropine sulfate 0.3 to 0.6 mg. It was given one hour prior to the beginning of anesthesia. A few patients received the premedication intravenously when scheduled for emergency operation. Meperidine (demerol®) hydrochloride was substituted for morphine sulfate in patients giving a history of sensitivity to the latter drug.

The types of operation varied widely, as illustrated in the following table.

Types of Operation

General surgery	470
Eye; ear, nose, and throat; genitourinary and dental surgery	255
Gynecologic surgery	585
Neurosurgery	450
Orthopedic surgery	415
Plastic surgery	325

4. Stoelting, V. K.; Graf, J. P., and Rasch, G.: Current Res. in Anesth. & Analg. **29**:61, 1950.

METHOD OF ADMINISTRATION

In this study, seconal® sodium was administered, without exception, by the intravenous route. Early in the investigation the total dose of the drug was arbitrarily set at 250 mg. and later was increased to 500 mg. This dosage was exceeded in only 22 patients, who received from 600 to 650 mg.

Patients in good condition were given 125 to 250 mg. of seconal® sodium at a single injection. If the degree of hypnosis was not obtained in three to five minutes, additional injections of 25 to 75 mg. of the drug were given at three to five-minute intervals until the desired degree of hypnosis was obtained.

After careful analysis of our results in the first 500 patients, the total dose of the drug was decreased to 250 mg. Patients not having the desired hypnosis with this dosage were given demerol® intravenously rather than additional amounts of seconal® sodium.

CLINICAL RESULTS

Nitrous oxide was the principal anesthetic agent in 1,800 patients. Seconal® sodium was the only supplementary adjunct in 960 patients. Eight hundred and forty patients received pentothal® sodium in addition to seconal® sodium. The amount of pentothal® required for adequate hypnosis, however, was much reduced.

The rate of flow of nitrous oxide and oxygen was maintained at 4 and 1.5 to 2 liters per minute, respectively. Patients requiring greater concentrations of oxygen were maintained on a mixture of 50% nitrous oxide and 50% oxygen, with the rate of flow being 3 liters per minute for each gas. The carbon dioxide absorption semiclosed circle or to-and-fro filter technique was used for the administration of the inhalation agents.

One hundred patients received cyclopropane in addition to seconal® sodium prior to intubation. All of these patients were then maintained on nitrous oxide.

Seventy-five patients received ethyl ether during the operation. These patients were requiring excessive amounts of pentothal® sodium for hypnosis after the initial dose of seconal® sodium, or were exhibiting overactive cough reflexes.

Five hundred and twenty-five patients under spinal anesthesia received seconal® sodium intravenously for hypnosis.

One hundred and thirty-five patients had not regained active reflexes before leaving the operating room. Seventeen hundred and seventy-five patients were awake, talking rationally, and obeying commands when removed from the operating room suites. These patients remained awake and cooperative after being returned to bed on the ward. Six hundred and twenty patients regained active reflexes but remained drowsy and sleepy for four to five hours after operation.

Of the 135 patients who had not regained active reflexes in the operating room, one died on the table after a massive hemorrhage, 14 received added ethyl ether, and 88 received 375 mg. to 650 mg. of seconal® sodium. Ten patients had cerebral explorations and remained mentally confused for several days. Only 22 patients receiving 250 mg. or less of seconal® sodium failed to recover active reflexes at the completion of the operation.

Two hundred and thirty patients had an initial drop in blood pressure within a period of 15 minutes after seconal® sodium was administered intravenously. This drop was greater in the systolic limb of the blood pressure. The systolic drop

varied from 10 to 60 mm. of mercury and averaged 28 mm. The diastolic drop was proportionately smaller and averaged 15 to 20 mm. This drop was transient, and the pressure returned to the preoperative level within 20 to 30 minutes in all except 22 patients. These 22 patients responded readily to vasopressor drugs. Forty patients experienced a rise in blood pressure. This rise occurred while the patients were being greatly stimulated. The pressure readily returned to the preoperative level after cessation of the stimulation.

Fifty-nine patients showed varying degrees of respiratory depression; 16 had received 600 mg. of seconal® sodium; 12, 375 mg.; 27, 250 mg., and 4 patients, only 125 mg. As with the other barbiturates, the depression was of short duration and was treated with artificial respiration using 100% oxygen (by manual compression of the rebreathing bag).

Intubation was performed in 830 patients in this study. Six hundred and forty-two patients were intubated nasally and blindly after adequate cocainization of the vocal cords. One hundred and thirty-eight were intubated orally and 50 were intubated nasally under direct vision. The latter 188 patients received dimethyl tubocurarine iodide [5] for relaxation of the mandibular and pharyngeal muscles. Mild laryngeal spasm developed in 38 patients after attempts at blind intubation. Dimethyl tubocurarine iodide, given intravenously, immediately relieved the laryngeal spasm.

In 53 patients severe pharyngitis developed after blind nasal intubations. Recovery from this complication occurred spontaneously without any special treatment.

POSTOPERATIVE COMPLICATIONS

Thirty-eight patients died after operation. Eight of these patients had undergone cerebral explorations, with removal or partial removal of brain tumors. Death was due to increased intracranial pressure and hemorrhage. These clinical observations were confirmed by postmortem examinations. One patient died of severe hemorrhage during the operation. A pulmonary embolus on the eighth to the tenth postoperative day accounted for four deaths. Eighteen patients died of carcinomatosis three to four weeks after surgery. In one patient a coronary occlusion developed 36 hours after operation. This patient had been given spinal anesthesia with seconal® sodium for hypnosis. The course of the anesthesia had been uneventful. Two patients with extensive burns died 7 to 10 days after skin grafting. Seconal® sodium was not considered a contributing factor in any of these deaths.

One hundred and eighty-five patients manifested varying degrees of nausea and vomiting after operation. These complications existed 24 to 48 hours after operation. Seconal® sodium may conceivably have been a contributing factor in this complication, but certainly to no greater extent than if some other barbiturate had been used.

Twenty-three patients complained of postoperative headache. Spinal anesthesia was considered the causative factor in 12 patients. Seconal® sodium was not considered the cause of this complication in the other 13 patients.

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5. Metubine iodide.

In 35 patients atelectasis developed 24 hours postoperatively. Upper abdominal operations had been performed in 34 of these patients. The other patient had undergone an intracranial neurolysis for carcinoma of the neck. Circulatory and respiratory collapse developed 48 hours after the operation, and the patient died within a few hours. Postmortem examination revealed pronounced cerebral edema as the cause of death.

Twenty-five patients had postoperative thrombophlebitis of varying degrees. This complication occurred in the early part of the study, in which salt of seconal® sodium in a 50% sucrose solution was used. No morbidity of this type has been observed with the use of seconal® sodium in the polyethylene glycol and water vehicle.

COMMENT

We have evaluated a known barbiturate which has been prepared in a different form and administered in a different manner. This drug should be used with the same precautions as the other barbituric acid derivatives. Seconal® sodium has been used in two different ways: first, for hypnosis with spinal anesthesia and, second, as a basal anesthetic drug, principally with nitrous oxide anesthesia.

Seconal® sodium, when administered in excessive quantities or too rapidly, has many of the disadvantages of the other barbiturates, principally respiratory depression and initial drop in blood pressure. Postoperative drowsiness was observed following the administration of extremely large doses of the drug or when the anesthesia time was less than one hour.

Most of the complications occurred in patients receiving more than 250 mg. of the drug. The total dose should be limited to 250 mg. and pentothal® sodium administered for additional hypnosis or demerol® intravenously for additional analgesia. Seconal® sodium should be reserved for cases in which the estimated anesthesia time is one hour or more. The number of patients not responding or exhibiting active reflexes immediately after completion of the operation will be reduced, if the above precautions are observed.

The advantages, like those of any intravenously administered barbiturate, are quick, pleasant induction, easy control of anesthesia, and a low incidence of postoperative nausea and vomiting.

During the past two years we have been treating all tetanus patients admitted to the Riley Hospital for Children with rectal and intravenous administration of seconal® sodium. These patients also received dimethyl tubocurarine iodide subcutaneously or intramuscularly every two to five hours, as needed, to provide the desired muscular relaxation. The Department of Anesthesiology was given full control of this treatment. All patients were evaluated, and the dosage of each drug was determined for each patient. During the course of treatment it was necessary to change both types of medication frequently to meet the requirements of the patients. Most of these patients underwent early tracheotomy in order to maintain adequately an airway and remove excess secretions.

Ten patients have been treated under this regimen in the last 24 months. All patients have recovered, with no residual complications. Prior to this method of treatment, the mortality rate in patients suffering with tetanus in the Riley Hospital had been over 50%. We feel that this form of treatment is wholly responsible for no deaths at the hospital in the last two years.

Seconal® sodium has a definite place in the armamentarium of drugs used by the anesthesiologist and certainly deserve further clinical investigation.

SUMMARY

Seconal® sodium has been administered intravenously, both in a 50% sucrose vehicle and in a polyethylene glycol and water vehicle, to 2,500 patients for basal hypnosis.

The main advantages were quick, pleasant induction, low incidence of laryngospasm, low incidence of postoperative nausea and vomiting, and long duration of action. The disadvantages were respiratory depression, initial hypotension, and postoperative drowsiness.

ABSTRACT OF DISCUSSION

DR. R. J. WHITACRE, East Cleveland, Ohio: We are indebted to Dr. Stoelting and Dr. Graf for calling our attention to a very useful drug and to the method of its administration.

Although in many centers secobarbital (seconal®) sodium or pentobarbital (nembutal®) has been used intravenously for a good many years, there are still anesthesiologists who have failed to take advantage of such use of these drugs. In regard to the use of seconal® itself, we have found it to be satisfactory, although there is no particular difference between it and nembutal® used intravenously. Indeed, we felt that it was perhaps just a little more cumbersome to use, because it seemed more viscid than nembutal.®

There are a couple of points which Dr. Stoelting brought out that I should like to reemphasize, because I think they are extremely important. Number one is the dose of the drug. The use of larger doses of seconal,® 300 to 500 mg. or more, causes an increase in undesirable side-effects. If we limit the amount of seconal® to 150 or 250 mg., at the most, we will find that the instance of satisfactory results will be increased.

We should also warn the enthusiastic user of these drugs that they should be used only to produce basal narcosis. Dr. Stoelting brought out that if the patient is having pain, the use of some other drug or agent should be considered.

One other point that Dr. Stoelting mentioned that I should like to emphasize is that these drugs are particularly useful to the anesthesiologist when there is need of a method of producing hypnosis quickly; also, they are particularly useful in operations that are going to last for a longer time.

DR. JAMES E. ECKENHOFF, Philadelphia: Dr. Stoelting and Dr. Graf have presented evidence that seconal® sodium has a real place in anesthesia, particularly when used to supplement nitrous oxide anesthesia for minor operations or to supplement spinal anesthesia. However, one should particularly note their advice on limiting the dose of the agent to 250 mg. This is another agent that is pleasant for the patient to take. That along with its ease of administration makes it a drug that can be used unwisely and promiscuously by the unwary. Unless its limitations are clearly stated at the outset, we may soon find it falling into disrepute such as did thiopental (pentothal®) sodium for a while and as curare is in certain quarters at present.

Our experience with the longer-acting barbiturates has caused us to eliminate them or use them cautiously in the elderly. Patients over 65 years of age not uncommonly show hypotension or respiratory depression and even Cheyne-Stokes respiration when barbiturates are administered. These are also the patients in whom atelectasis and other respiratory complications are more likely to develop and who therefore must be given barbiturates sparingly.

The incidence of 35 cases of postoperative atelectasis in 2,500 patients, or 1.4%, as cited by Dr. Stoelting is high, and one can but speculate on whether the barbiturate is responsible. An inspection of our records at the Hospital of the University of Pennsylvania for the past year indicates that we have had 35 cases of postoperative atelectasis in 7,400 cases, or an incidence of 0.47%. I should like to ask Dr. Stoelting if he has compared the incidence of atelectasis in a similar operative group that did not receive seconal® sodium. The mere fact that 34 of the 35 cases of atelectasis involved patients who underwent upper abdominal operations suggests that a longer-acting barbiturate is not a drug to use when such surgery is contemplated.

As pointed out in this report, seconal® may depress the respiration and cause the blood pressure to fall. With spinal anesthesia there is a decrease in respiratory minute volume and a tendency to hypotension. When the spinal anesthesia is to be supplemented with administration of seconal,® one should remember that the effects of the two may be additive.

Finally, the report of the use of seconal® sodium in the treatment of tetanus is of particular interest and importance. Certainly a record of no deaths in 10 cases of tetanus is an enviable one.

DR. J. P. GRAF, Indianapolis: I wish to thank the discussants for their comments and suggestions. In partial answer to Dr. Whitacre's question about the vehicle, at the present time the manufacturers are just beginning to produce a new vehicle which they state is thinner than water. As yet we know nothing about the composition of it and, of course, know as little about how it is going to work or if it will cause any complications. However, this may be the answer to the clumsiness in the use of the drug.

In answer to the question about the incidence of atelectasis, we have not had a comparable series of patients given other types of anesthesia. However, it has been our feeling that perhaps our over-all incidence of atelectasis does run higher than in some hospitals, in part owing to the fact that our upper abdominal operations are frequently extremely long. We have also felt that in some cases we were overenthusiastic in giving postoperative sedation.

I should like to emphasize once more that we feel that the two most important things are, first, to limit the dosage of the drug and, second, not to use it in operations which are not expected to last over an hour. I should also like to urge other anesthesiologists to try this drug in the treatment of tetanus. We have been gratified with the results and would be interested to know if anyone else has used it and what results have been obtained.

FOLLOW-UP STUDIES FOLLOWING TOTAL PELVIC VISCERECTOMY

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IT IS BECOMING apparent that total pelvic viserectomy with ureterointestinal anastomosis is a feasible operative procedure for certain pelvic neoplasms.[1] Though the operation is severe and the mortality rate considerable, the procedure affords certain patients palliation and the possibility of "cure" in circumstances which would have been considered hopeless a few years ago. Our present interests are concerned with the selection of cases and the results of the procedure.

This presentation covers an experience with the radical operation, that is, total removal of pelvic viscera and pelvic lymph nodes en bloc. Partial viscerectomies have been carried out for many years, and they and radical Wertheim operations are not considered in this report.

The total viscerectomy as now carried out consists in either abdominal-perineal or supralevator resection with terminal sigmoid colostomy and anastomosis of ureters to colon. Usually the right ureter is anastomosed to cecum or ascending colon and the left ureter is anastomosed to sigmoid colon. A simple nontunneled, end-to-side ureterointestinal anastomosis is utilized. As in most instances the pelvic peritoneum is widely sacrificed, pelvic reperitonealization is usually not possible, and it is probably unnecessary. The operation ordinarily lasts from two to three hours, and on the average 3,000 cc. of transfused blood is required. Intra-arterial transfusion has been of unusual benefit in instances in which it has been employed because of rapid and severe bleeding during operation. Consideration is being given to employing it as a routine technic in operations of this type. Early in the operation the hypogastric arteries are ligated to minimize blood loss and the hypogastric veins are ligated both to lessen venous bleeding and to reduce the incidence of postoperative pulmonary embolism.

From the Department of Surgery, College of Medicine, State University of Iowa (Dr. E. S. Brintnall, Associate Professor).

1. (*a*) Brunschwig, A.: Complete Excision of Pelvic Viscera for Advanced Carcinoma, Cancer **1**:177-183 (July) 1948. (*b*) Brintnall, E. S., and Flocks, R. H.: En Masse "Pelvic Viscerectomy" with Uretero-Intestinal Anastomosis, Arch. Surg. **61**:851-868 (Nov.) 1950. (*c*) Brunschwig, A., and Pierce, V. K.: Partial and Complete Pelvic Extenteration, Cancer **3**:972-974 (Nov.) 1950. Bricker, E. M., and Modlin, J.: The Role of Pelvic Evisceration in Surgery, Surgery **30**:76-93 (July) 1951.

Total pelvic viscerectomy has been carried out in 27 patients during the past four years.[2] Sixteen patients had locally extensive rectal or rectosigmoid cancers, and 10 patients had cancer of the cervix, recurrent after irradiation therapy. In one patient there was an unusual extension of prostatic cancer to bladder and rectum which required this procedure. It is of interest that in five instances of extensive carcinoma of the ovary or of the body of the uterus none was removable by total pelvic viscerectomy. If such cancers were sufficiently invasive locally to justify the operation, there was invariably spread beyond the field of operability. During this four-year period exploration was carried out in about an equal number

TABLE 1.—*Operative Mortality (Eight Patients—30%)*

Cardiac failure	2
Pulmonary embolism	3
Irreversible shock	1
Cerebral infarct	1
Uremia and atelectasis	1

TABLE 2.—*Short-Term Survivals (Nine Patients—33%)*

Death from recurrence	3
Pyelonephritis	2
Fecal fistula or intestinal obstruction *	4

* All four patients had intensive irradiation for carcinoma of the cervix.

TABLE 3.—*Present Surviving Patients (10 Patients—37%)*

Patient	Age	Lesion	Survival, Mo.
E. M.	53	Carcinoma of rectum	48
A. A.	63	Carcinoma of rectum	36
E. D.	34	Carcinoma of cervix	33
M. B.	48	Carcinoma of cervix	30
L. K.	54	Carcinoma of rectum	12
C. C.	55	Carcinoma of cervix	6
J. W.	66	Carcinoma of rectum	6
E. J.	57	Carcinoma of rectum	5
W. P.	47	Carcinoma of rectum	4
V. H.	74	Carcinoma of prostate	1½

of patients with the intention of performing total pelvic viscerectomy, but they were not subjected to the operation because of extension of the neoplasm beyond the limits of the pelvis. We believe that the procedure should not be carried out unless it will remove all gross carcinoma.

Eight patients died within one month after operation, giving an operative mortality rate of 30%. There were no deaths on the operating table.

Nine patients died 1 to 18 months after operation and are considered to have had short-term survivals. Three of these nine patients were completely restored to normal health and activity for many months before death, and in them the operation afforded real palliation and prolongation of life.

2. Nine patients with extensive carcinoma of rectum and sigmoid colon included in this series were previously reported in the ARCHIVES.[1b]

At this writing, 10 patients are living and well from 2 to 48 months after operation. Four of them represent survivals of more than 30 months after operation.

The patients who survive the operation are generally freed of pain and lead normal lives despite the "wet colostomy" which requires the use of a "glue-on," ileostomy-type bag. In general the renal complications are not excessive, and in only one patient who survived the operation has there been a tendency toward chronic acidosis. Patients who recover from the operation only to die many months later of recurrence and metastasis have good palliative relief and lead essentially normal lives up to a final period of rapid deterioration.

From the results in this series it would seem that the operation of total pelvic viscerectomy is of real value to patients with certain extensive pelvic cancers, affording definite palliation for many patients and the possibility of "cure" for some.

RECURRENT CANCER OF THE COMMON BILE DUCT AND PERIAMPULLARY REGION

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THE PROBLEM of recurrent cancer in the upper gastrointestinal and biliary tracts has not created the surgical unrest that equally malignant lesions on the surface of the body or in the musculoskeletal system have evoked. The defeatist attitude regarding the prognosis following the reresection of gastric cancer has been manifest in cancer producing biliary obstruction, and most surgeons do not feel justified in performing an operation in either area for recurrence offering a major risk of morbidity or mortality. It is an incontrovertible fact that the radical operation for neoplastic biliary obstruction is attended by a high mortality rate and a discouraging salvage. As previously stated in regard to the problem of resection in the face of recurrence of gastric cancer,[1] secondary resections of locally recurring lesions afford patients greater comfort with a more extended span of life than other surgical and nonsurgical methods of palliation and in an occasional instance control of an otherwise hopeless cancer.

A unique experience has allowed us to study the development of cancer in the periampullary area arising in the common duct and to assess the complications and sequelae of transduodenal local excision. With the standardization of the radical approach of the Whipple operation and the greater security consequent to improvements in antibiotics, parenteral electrolytic replacement therapy, and the use of larger volumes of blood in forestalling shock, a review of the indications for transduodenal local excision has seemed in order.

THE PROBLEM OF LOCAL EXCISION FOR PERIAMPULLARY CANCER

Halsted [2] in 1900, in the first reported case of local excision of a cancer in the ampulla, describes the experience which has been far commoner than is recognized in "favorable cases." His patient had an unresectable local recurrence on exploration a little over two months after a wide local resection. In discussing the problem, he stated:

> The result in this case is not encouraging, for it was my opinion at the time of operation that the case could not have been more favorable. But I did in this case what I never do if it can be avoided, namely, cut well down to or perhaps a little way into the new growth for the sake of diagnosis. . . . We must learn to make the diagnosis in other ways.

From the Gastric Service of the Memorial Cancer Center.

1. McNeer, G.; Booher, R. J., and Bowden, L.: The Resectability of Recurrent Gastric Carcinoma, Cancer **3**:43-55, 1950.

2. Halsted, W. S.: Contributions to the Surgery of the Bile Passages, Especially of the Common Duct, Bull. Johns Hopkins Hosp. **11**:1-11, 1900.

Halsted's observation on the reason for dissemination of this tumor is worthy of note in the light of a recent suggestion by Cole [3] to explain an early recurrence of a favorable lesion. This author felt that with malignant cells found free in the obstructed duct of Wirsung dissemination of cancer could be attributed to cutting across the pancreatic duct during subtotal pancreatoduodenectomy and allowing the escape of fluid-bearing tumor cells into the operative site. It seems reasonable for Cattell and Pyrtek [4] to use this as one of their arguments in consideration of a total pancreatectomy in cancers arising in the pancreas, as opposed to subtotal procedures.

The operative philosophy of transduodenal local excision was clearly presented by Orr [5] in 1941, after assessing Hunt's review. He contrasted Outerbridge's [6] series of patients without treatment who survived an average of 7.3 months, Judd and Parker's [7] series who underwent palliative biliary-intestinal anastomosis and survived 7.7 months (a later report [8] gave an average survival time of 13.9 months) as opposed to an average postoperative survival of 25.8 months for transduodenal excision of carcinoma of the ampulla of Vater, and Pack and McNeer's [9] series, in which there was an average survival period of 8 months after palliative high-voltage x-ray therapy, with the 30 patients in Hunt's series who were dead, averaging 1.7 years' survival, and the 34 patients surviving at the time of the report for an average of 2.5 years. He stated that

> the choice of transduodenal or Whipple operation should depend on the extent of the lesion found at operation. With the recorded excellent results of the former technic we must assume that the more radical procedure is not necessary when the tumor is small and confined to the ampulla. However, the Whipple technic more nearly fulfills the requirements of an operation for carcinoma, in that the region of early extension of the tumor is removed. Carcinoma, arising in the pancreas and involving the common duct or ampulla, is suitable only for the Whipple operation.

The cumulative experience with transduodenal or retroduodenal excisions of peripapillary tumors has been summarized by Cohen and Colp,[10] Hunt and Budd,[11] and Whipple [12] and finally brought to date in 1941 by Hunt.[13] Review of this data reveals, however, that the operation presents many limitations. It is significant that of 86 patients surviving the operation, 12, or 14%, were living and well

3. Cole, W. H., quoted by Cattell and Pyrtek.

4. Cattell, R. B., and Pyrtek, L. J.: An Appraisal of Pancreatoduodenal Resection: A Follow-Up Study of 61 Cases, Ann. Surg. **129**:840-849, 1949.

5. Orr, T. G., in discussion on Hunt, Ann. Surg. **114**:601-602, 1941.

6. Outerbridge, G. W.: Carcinoma of the Papilla of Vater, Ann. Surg. **57**:402-426, 1913.

7. Judd, E. S., and Parker, B. R.: Biliary Intestinal Anastomosis for Obstructive Jaundice: Analysis of 137 Consecutive Cases, Arch. Surg. **17**:1-17 (July) 1928.

8. Judd, E. S., and Hoerner, T. M.: Surgical Treatment of Carcinoma of the Head of the Pancreas and of the Ampulla of Vater, Arch. Surg. **31**:937-942 (Dec.) 1935.

9. Pack, G. T., and McNeer, G.: Radiation Treatment of Pancreatic Cancer, Am. J. Roentgenol. **40**:708-714, 1938.

10. Cohen, I., and Colp, R.: Cancer of Periampullary Region of the Duodenum, Surg., Gynec. & Obst. **45**:332-346, 1927.

11. Hunt, V. C., and Budd, J. W.: Transduodenal Resection of the Ampulla of Vater for Carcinoma of the Distal End of the Common Duct, Surg., Gynec. & Obst. **61**:651-661, 1935.

12. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, Ann. Surg. **102**:763-779, 1935.

13. Hunt, V. C.: Surgical Management of the Ampulla of Vater and of the Periampullary Portion of the Duodenum, Ann. Surg. **114**:570-600, 1941.

TABLE 1.—*Secondary Resection After Local Excision of Peripapillary Cancer*

	Surgeon, Year	Sex, Age	First Operation	Second Operation	Result
1.	Rixford * 1901	Female 33	11/22/1899, cholecystostomy, one month later transduodenal excision of adenocarcinoma of ampullary area	30 days later, wider excision with retroperitoneal nodes; reimplantation of ducts	Died 7 mo. after last operation, 8 mo. after resection
2.	Lumêris † 1912	Male 44	11/23/1907, resection, cholecystectomy, drainage of hepatic duct	8/27/1908, resection of recurrent lesion, partial excision of liver, drainage of hepatic duct	Died 8 mo. after the second operation
3.	Santero ‡ 1934	Male 50	10/10/1927, one-stage transduodenal excision for adenocarcinoma	3/16/1929, recurrence in 17 mo.; second radical excision	Died 22 mo. after the first operation

* Rixford, J. E.: J. A. M. A. **36**:1492-1493, 1901.
† Lumêris, H. J.: Zentralbl. Chir. **39**:1665-1667, 1912.
‡ Santero, N.: Arch. ital. chir. **36**:191-216, 1934.

TABLE 2.—*Reexploration for Recurrence After Local Resection of Periampullary Cancer*

	Surgeon, Year	Sex, Age	First Operation	Second Operation	Result
1.	Halsted # 1900	Male 60	2/14/1898, resection of common duct, pancreatic duct, and portion of duodenum	5/5/1898, 3 mo. later cystoduodenostomy for recurrence	Died in the fall of 1898
2.	W. J. Mayo * 1901	Female 59	11/3/1900, cholecystostomy 1/3/1901, transduodenal excision "partly by cautery"	7/7/1902, 18 mo. later, cholecystoduodenostomy for recurrence	Died 4 mo. after last operation, 22 mo. after resection
3.	Kausch † 1912	Male 49	6/15/1909, cholecystoenterostomy. 8/21/1909, resection of 11 cm. of duodenum and part of pancreas. Pancreaticoduodenostomy and gastroenterostomy	5/25/1910, cholecystostomy for recurrence	Died postoperatively, 9 mo. after resection
4.	Bohm ‡ 1914	Male 52	5/10, local excision of hazelnut-sized adenocarcinoma of ampulla	Reoperated on 2 yr. later for local recurrence, gastroenterostomy	Lived 1 yr. after the second operation, 3 yr. after resection
5.	Muller and Rademaker § 1931	Male 52	5/20/1924, transduodenal excision, choledochoduodenostomy	8/17/1926, cholecystoduodenostomy. 3/11/1927, gastroenterostomy	Died 4 yr., 8 mo. after resection. "Pulmonary metastases," with epigastric tumor mass
6.	Judd ‖ 1932	..	12/21/1928, transduodenal excision of carcinomatous polyp of ampulla after preliminary choledochostomy and cholecystostomy	9/9/1929, cholecystogastrostomy. 4/26/1931, gastroenterostomy	Alive 2 wk. after last operation and 29 mo. after excision
7.	Pemberton ¶ 1932	Male 44	1/10/1925, cautery transduodenal excision of colloid cancer developing in papillary adenoma	9/20/1926, reexplored; extensive metastases	Died 20 mo. after excision
8.	Cabot ∠ 1933	Male 35	1925, transduodenal excision for "robin's egg"-sized cancer of ampulla	4 yr. later, cholecystectomy for empyema of gallbladder; tube used for reimplanting duct still in duodenum and "was not disturbed"	In 1933 alive without evidence of disease 8 yr. postoperatively
9.	Santero ** 1934	Female 72	7/1/1928, transduodenal excision, implantation of common and pancreatic ducts into duodenum	10/30/1929, cholecystostomy	Died 19 mo. after first operation
10.	Bengolea †† 1935	Female 37	Choledochotomy and cancer locally excised through it; drainage of duct	Reoperation in 3 mo., metastases in node	.....
11.	Gordon-Taylor ‡‡ 1942	Female 55	1925, retroduodenal removal of "papillomatous outgrowth" within duct	"Some months" later a palliative gastrojejunostomy for recurrence	Died about 1 yr. after primary intervention
12.	Gray and Sharpe §§ 1943	..	3/16/1940, transduodenal excision, new cholecystogastrostomy replacing one made 9 mo. before	11/19/1941, gastroenterostomy for recurrence	Died 22 mo. after resection

* Reported by Walters, W., and Snell, A. M.: Diseases of the Gallbladder and Bile Ducts, Philadelphia, W. B. Saunders Company, 1940, p. 480.
† Reported by Lieber, Stewart and Lund.[10]
‡ Reported by Hunt.[13]
§ Ann. Surg. **93**:755-760, 1931.
‖ Cited by Walters, W.: Surg., Gynec. & Obst. **55**:648-651, 1932.
¶ Cited by Walters, W.: Surg., Gynec. & Obst. **55**:648-651, 1932.
∠ Cited by Potter, E. B.: Ann. Surg. **98**:369-373, 1933.
** Arch. ital. chir. **36**:191-216, 1934.
†† Reported by Whipple, Parsons, and Mullins.[12]
‡‡ Brit. M. J. **2**:119-121, 1942.
§§ Surgery **14**:831-846, 1943.

for periods varying from 3 to 22 years, but in 26, or 30%, death occurred from recurrence or metastases in one year or thereabouts, several patients surviving for two and one-half to three years.

In these surveys, two groups of cases merit reconsideration on the basis of findings at reexploration. The most interesting group is a small one in which reexploration revealed a resectable recurrent lesion. These cases are summarized in Table 1, though the cancer in the second case, that of Laméris, is in the upper segment of the common duct and, anatomically speaking, is a little above our problem, which concerns the periampullary area, though it shows the difficulty, here a necessity, of local excision operations.

A much larger series of patients underwent secondary exploratory procedures with or without palliative decompression of the biliary or gastrointestinal tracts, but without resection. The data are summarized in Table 2.

That recurrence after local excision of peripapillary cancer is not unexpected has been most recently demonstrated by Miller, Dockerty, Wollaeger, and Waugh,[14] who showed that in 10 (76.9%) of 13 instances in which transduodenal excision was performed malignant cells were noted at the periphery of the sectioned specimen. Of the 13 patients, only one survived for three years, and this patient had recurrence of his cancer. While there are isolated examples of favorable results with this operation, the number of local failures in obviously early and favorable cases would indicate that consideration of the isolated instances has taken precedence over consideration of the more constant sequel of local excision, that is, local recurrence. The problem is presented of whether "small operations" are to be fitted to "small cancers" in the philosophy of cancer surgery.

An unusual example of a long silent but still resectable local recurrence of a favorable periampullary cancer follows.

REPORT OF A CASE

S. Z., a 74-year-old Jewish man, was admitted to the Memorial Hospital on July 3, 1950, complaining of pruritus. Four weeks previously an episode of vomiting, sore throat and chills developed, for which penicillin was thought to have relieved him in a day, and with a recurrence of the fever one week before his admission, aureomycin was given. Jaundice and itching then appeared.

The relevant past history was the matter of a report in the ARCHIVES in July, 1943.[15] On April 29, 1946, a local excision with reimplantation of the common bile and pancreatic ducts had been done. The diagnosis was adenocarcinoma of the ampulla of Vater, Grade II, the site of origin being manifest in the wall of the common duct (Fig. 1).

A significant interval finding was shown in a gastrointestinal series done in May of 1947, showing a reflux of barium sulfate into the common duct for a distance of 4 cm. (Fig. 2*A*), but acrophagia was his only complaint.

Physical examination revealed obvious scleral icterus. The blood pressure was 120/60 mm. of mercury, and the pulse rate was 70. His weight was 163 lb. (74 kg.). There was no evidence of fever at any time. The patient had a well-healed, transverse upper right quadrant scar. The

14. Miller, E. M.; Dockerty, M. B.; Wollaeger, E. F., and Waugh, J. M.: Carcinoma of the Region of the Papilla of Vater: A Study of Cases in Which Resection Was Performed, Surg., Gynec. & Obst. **2**:172-182, 1951.

15. Pack, G. T., and Booher, R. J.: Surgical Problem of Periampullary Cancer, Arch. Surg. **57**:71-103 (July) 1943.

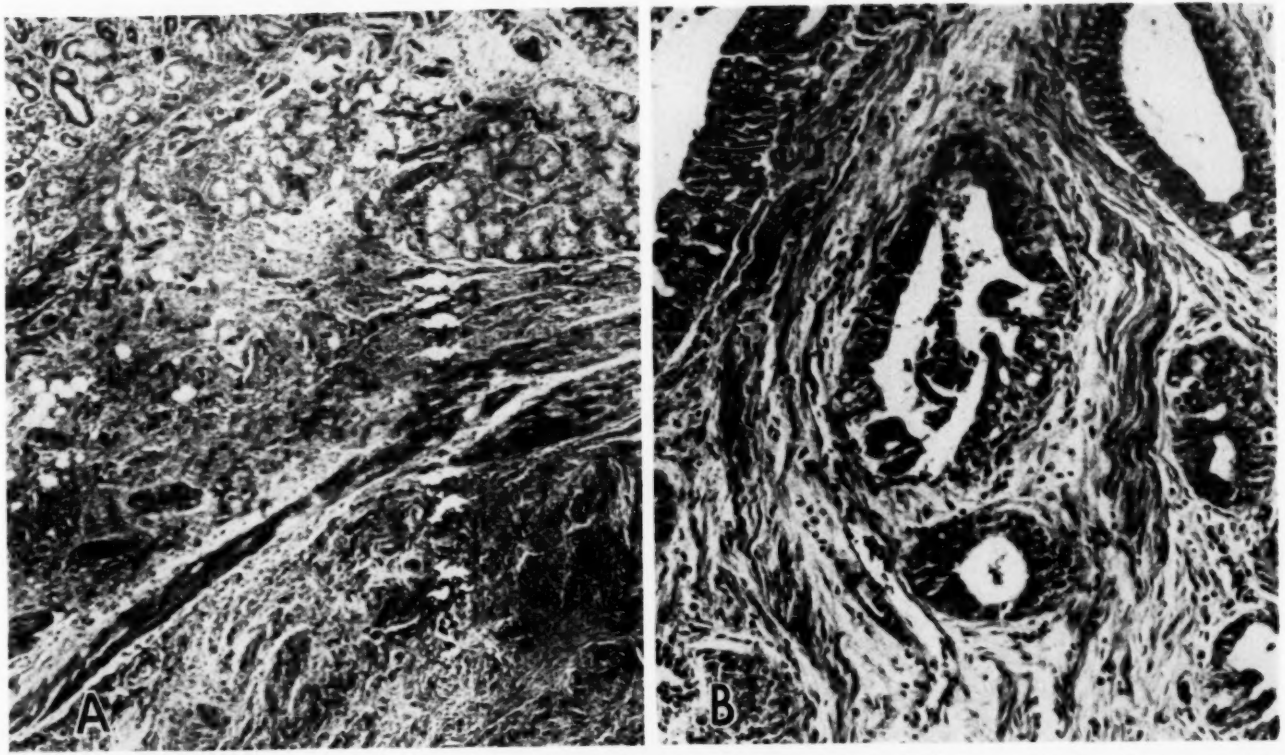

Fig. 1.—*A*, photomicrograph showing small focus of cancer deep in the wall of the common duct. *B*, higher magnification showing an adenocarcinoma of grade II histological malignancy.

liver edge was just palpable, and it was questionable whether the gall bladder could be palpated. Except for a suprapubic cystostomy scar, the remainder of the examination revealed no abnormalities.

Laboratory studies revealed a hemoglobin content of 12.3 gm. and a hematocrit value of 42. The quantitative van den Bergh test revealed 2.78 mg. of serum bilirubin per 100 cc., with a direct component of 1.92 mg. The alkaline phosphatase was 21.52 Bodansky units and the serum cholesterol 260 mg. per 100 cc., with 182 mg. the value for the esterified form. The total protein was 7.8 gm. and the serum albumin 3.5 gm. Cephalin flocculation was negative at 48 hours, and the thymol turbidity was 1.46. Stool examination showed occult blood present on two occasions. Duodenal drainage was negative for neoplastic cells and was considered to be in Class I.

A gastrointestinal series showed a smooth narrowing 1.5 cm. distal to the duodenal bulb which was felt to represent stenosis subsequent to operation rather than recurrent disease (Fig. 2*B*). Several small bowel loops just distal to the ligament of Treitz were thought to be held there by adhesions, but the presence of a mass in this area was suggested.

Because of the roentgenographic evidence of stenosis of the common duct three years previously, the tentative preoperative diagnosis varied between recurrent cancer and biliary duct stenosis.

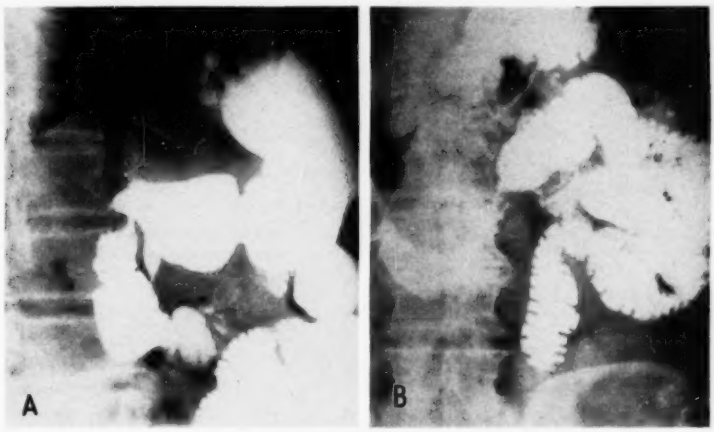

Fig. 2.—Gastrointestinal roentgenograms made (*A*) one year after reimplantation of the common duct, showing a reflux of barium into the duct, and (*B*) three years later, showing stenosis of the duodenum and several adherent loops of small bowel just distal to the ligament of Treitz, with the suggestion of a mass in this area.

The patient was therefore subjected to exploratory laparotomy on July 10, and a hard mass was found in the head of the pancreas overlying the third portion of the duodenum with extension into the uncinate process. A small lymph node found at the inferior angle of the common bile duct and duodenum was excised, and frozen-section study revealed an adenocarcinoma. There were numerous adhesions of small bowel to jejunum at the base of the mesentery and over the duodenum, and the common bile duct was dilated to a diameter of approximately 2 cm., with a very thick wall.

Pancreaticoduodenal resection was done, the greatest difficulty encountered being that of freeing the uncinate process from beneath the superior mesenteric vein. An end-to-end choledochojejunostomy and an oralis totalis, end-to-side antiperistaltic (anatomical) gastrojejunostomy were done. At the completion of this much of the procedure, the patient was in shock, and the operation was concluded hastily, with catheter drainage of the rather thick and edematous gall bladder and through-and-through closure of the abdominal wall. A pancreatic fistula was established on the sixth postoperative day. While the patient's condition was good, he was extremely negativistic. He continued to lose weight and by the 12th postoperative day was lethargic and weak despite all parenteral therapy. He was restrained from removing an orojejunal feeding tube and

was given a formula which netted over 3,000 calories per day. At the time of his discharge, on the 28th postoperative day, he was coming into positive nutritional balance, though he had lost a total of 22 lb. (10 kg.).

The pancreatic fistula closed approximately two months after the operation. The patient regained his weight slowly and was without symptoms until January of 1951, when he first noted dysphagia. A gastrointestinal series showed a little delay at the cardia, which was considered to be due to cardiospasm, while the gastroenterostomy functioned normally. There was a suggestion of a mass deep in the epigastrium. Hospitalization was again advised for diagnostic study, but the patient refused further examinations.

The pathological specimen consisted of the lower third of the stomach, the entire duodenum, a portion of the common bile duct and a large segment of attached omentum. The over-all

Fig. 3.—Photograph of the gross specimen, opened along the greater curvature and revealing an indurated ulcerated cancer around the stenotic common duct orifice.

measurements were 13 by 9 by 4 cm. Examination of the duodenum revealed the presence of an irregularly-shaped indurated ulcer, surrounding the ampullary orifice and measuring 2 cm. in its widest dimension. The borders of the ulcer were raised, hard and hemorrhagic. The common duct orifice was greatly narrowed, being constricted by encircling tissue, but it did permit the passage of a small probe into the duct. The open circumference of the common duct was 3.5 cm. The head of the pancreas was lobulated.

Multiple sections through the tumor revealed whitish, slightly hemorrhagic tumor tissue poorly encapsulated, infiltrating the head of the pancreas for a distance of 1.5 cm. There was a sharply circumscribed tumor lying adjacent but not in continuity with the primary tumor mass at the head of the pancreas, measuring 1 cm. in diameter.

The diagnosis was adenocarcinoma of the head of the pancreas (Fig. 4), with invasion of the duodenum and partial obstruction of the ampulla of Vater and lymph node metastases. Review

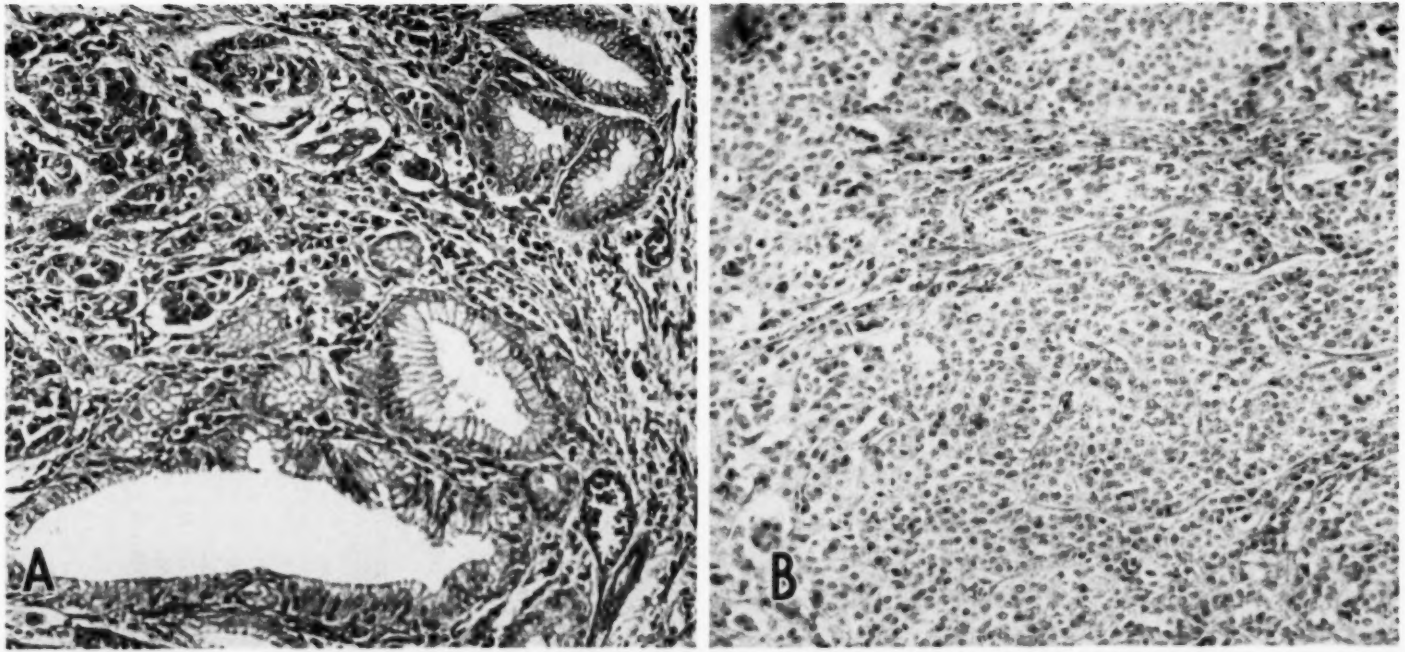

Fig. 4.—*A*, photomicrograph of the adenocarcinoma infiltrating along the wall of a pancreatic duct. *B*, photomicrograph of the adenocarcinoma arising in the common duct with a greater degree of anaplasia than was manifest in initial specimen from local excision.

of the initial specimen revealed that the tumor was histologically compatible with that removed at the preliminary resection, which was an adenocarcinoma shown to arise from the distal end of the common duct. The recurrent lesion was more malignant in appearance, however.

CANCER OF THE COMMON BILE DUCT

When the second surgical specimen was studied by the pathologist, the lesion had extended to a point at which the anatomical site of origin could not be determined. On histological study, it was felt to be an adenocarcinoma of the head of the pancreas with invasion of the duodenum, but the exact diagnosis was made after a review of the original material. This case exemplified Lieber, Stewart, and Lund's [16] statement that while cancer can arise from the epithelial lining of any of the structures which make up the ampulla and papilla it early permeates the surrounding structures and by extension soon involves adjacent structures to obscure the exact point of origin of the lesion. It is possible to classify each case only on the basis of extent of involvement at the time of examination. To emphasize the importance of detailed study and the reporting of early lesions in order to accumulate precise data for the interpretation of the results of the applied surgical procedures, it is well to restate these authors' detailed analysis of the 222 acceptable cases accumulated from the literature and from their own experience. In 182 cases all the epithelial structures of the papilla were involved, and in 33 all structures except the overlying mucosa of the papilla were invaded, while only one tumor could be considered to be definitely arising in the ampulla itself, three arose in the terminal duct of Wirsung, seven arose from the epithelium of the terminal bile duct, and four were from the intestinal mucosa covering the papilla itself. It is apparent that at the time the preponderance of these cancers were studied surgical relief had been delayed so long that the lesion, which almost universally is acutely and distressingly manifest to patient and physician alike, had spread beyond its site of origin.

In Stewart, Lieber, and Morgan's [17] subsequent report on cancer of the extrahepatic bile ducts, only 21 of 86 cases compiled were acceptable for study. While Marshall [18] had found that the commonest sites of the tumors of the bile ducts were at the lower end of the common bile duct and the ampulla of Vater, these authors found that of the 17 lesions that could be definitely located as to point of origin the largest group, 7, were at the lower end of the duct, but the remainder occurred with equal numbers in the upper and central thirds of the duct. While the lesions arising in the lower two-thirds of the duct probably present a common surgical problem, some of those in the upper third and those invading the juncture with the common hepatic and cystic ducts are to be considered separately as lesions amenable to resection with subsequent reimplantation of common hepatic or right and left hepatic ducts into the duodenum or a defunctionalized loop of jejunum and as such are beyond our consideration. In 12 cases the growth was localized, varying from "pea-size" to "hen's egg" in size. Nine of the lesions were stenosing

16. Lieber, M. M.; Stewart, H. L., and Lund, H.: Carcinoma of the Peripapillary Portion of the Duodenum, Ann. Surg. **109**:383-429, 1939.

17. Stewart, H. L.; Lieber, M. M., and Morgan, D. R.: Carcinoma of the Extrahepatic Bile Ducts, Arch. Surg. **41**:662-713 (Sept.) 1940.

18. Marshall, J. M.: Tumors of the Bile Ducts, Surg., Gynec. & Obst. **54**:6-12, 1932.

in type, and six were ulcerated. In 11 of these cases, metastases or extension had occurred, in contrast to Dick's [19] finding that 11 of 13 such lesions at necropsy showed no extension beyond the wall of the choledochus and no extension or metastases in other organs.

These reports do not manifest the importance of the lower common duct in relationship to the other epithelial sites of origin for neoplastic biliary obstruction. Ransom [20] has indicated its importance in the over-all picture by an analysis of 30 necropsies in which the histologic and anatomic sites of origin could be determined occurring in 158 cases with a final diagnosis of carcinoma of the pancreas; 8, or 26.6%, occurred in the common duct (five of these being completely localized) as opposed to five in the ampulla of Vater.

Neibling, Dockerty, and Waugh [21] have summarized the experience with carcinoma of the extrahepatic bile duct at the Mayo Clinic in the 40 years from 1907 to 1946 and found 29 lesions, or 32%, in the common duct out of a total of 90 in the extrahepatic ducts, while 26% were in hepatic ducts, 35% were at the juncture of common, cystic and hepatic ducts, and 3% were in the cystic duct. Recognition of this high incidence of cancer arising in the common duct is important in the management of those growths, which, when found at operation, have become extensive and have infiltrated pancreas and surrounding structures. Many such lesions, with biopsy of pancreas and bile ducts remaining comparatively unpracticable, may be considered primary in the pancreas on the basis of palpation, and because of the poorer prognosis in lesions having such a histological origin the surgeon may decide on palliative operations in cases which present better prognoses than he suspects.

In these earlier groups of cases there was a little variation in prognosis. Marshall found that the average duration of life after palliative drainage was 20 months, one patient living four years and three months after cholecystogastrostomy. In Stewart, Lieber, and Morgan's series, the survival was from 1 to 11 months after the onset of jaundice in the 13 patients treated medically, the average being 4.4 months as opposed to an average of 2.2 months of life for 8 patients treated surgically. The operative mortality over a period of 10 years or more ago, however, is hardly a compelling argument in the evaluation of this problem in consideration of the more effective postoperative armamentarium of the surgeon today.

No better classification of lesions of the bile ducts has been offered than that of Ewing.[22] He considers three types of lesions as follows:

1. Villous growths which may be single or multiple and which may fill and distend the duct. While they are uncommon, failure to be aware of the compiled experience of these lesions, which apparently are so favorable for a localized

19. Dick, J. C.: Carcinoma of the Lower End of the Common Bile-Duct, Brit. J. Surg. **26**:757-763, 1939.

20. Ransom, H. K.: Carcinoma of the Pancreas and Extrahepatic Bile Ducts, Am. J. Surg. **40**:264-281, 1938.

21. Neibling, H. A.; Dockerty, M. B., and Waugh, J. M.: Carcinoma of the Extrahepatic Bile Ducts, Surg., Gynec. & Obst. **89**:429-438, 1949.

22. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, Ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 754-755.

resection, may allow the surgeon to temporize in this instance more than in any other. Appearances may be corroborated by deceptive results of biopsies. A review of remarkable individual experiences with such cancers by Hansen,[23] Potter, Dick, Gordon-Taylor, Harvey and Oughterson,[24] Child,[25] and Cattell and Pyrtek[26] emphasizes that while the superficial villous structures may even appear benign there is adenocarcinomatous invasion in the base of the stalk and the adjacent wall of the duct, possibly with nodal metastases. The usual experience of prompt recurrence of such lesions indicates the futility of small operations for small cancers and removes this group from those lesions adapted to local procedures because of "apparent confinement."

2. A nodular form in which masses appear in the submucosa and muscular wall. They tend to encircle and constrict the passage early and may appear as cicatricial stenosis. Neibling, Dockerty, and Waugh have noted that the majority of lesions were of this type and appeared as circumscribed, firm, infiltrated, grayish-white nodules, often obstructing the lumen of the resected duct and associated with dilatation proximally. Because of their manifest infiltration, they are not to be considered locally resectable.

3. A more diffuse type of growth may extend along the duct, converting it into a smooth rigid tube, from the inner surface of which project minute carcinomatous vegetations. These lesions are commonly mistaken for common duct fibrosis and must be routinely remembered in explorations of the common duct and in assaying the cause of duct fibrosis and stricture exemplified by recent reports by Killins[27] and by Saypol and Fishman.[28]

Pickrell and Blalock[29] in 1944 summarized the attempts at removal of lesions definitely determined to be of bile duct origin, excluding those cases in which transduodenal excision was employed, and added two cases of their own to bring the total to 22. In this group, there were six postoperative deaths, two patients were untraced, one was alive and well at 60 (this patient's lesion was in the proximal end of the duct invading the area of juncture of the ducts), one at 18 and one at 7 months, and in the remaining 11 cases the postoperative survival was 12.6 months. Brunschwig and Bigelow[30] report a case in which they reexplored 11 months after excision of a portion of the extrahepatic bile ducts and the right lateral portion of the head of the pancreas but could not resect the recurrent lesion, which

23. Hansen, A. S., cited by Hunt and Budd.[11]

24. Harvey, S. C., and Oughterson, A. W.: The Surgery of Carcinoma of the Pancreas and Ampullary Region, Ann. Surg. **115**:1066-1085, 1942.

25. Child, C. G., III.: Pancreaticojejunostomy and Other Problems Associated with the Surgical Management of Carcinoma Involving the Head of the Pancreas: Report of 5 Additional Cases of Radical Pancreaticoduodenectomy, Ann. Surg. **119**:845-855, 1944.

26. Cattell, R. B., and Pyrtek, L. J.: Premalignant Lesions of the Ampulla of Vater, Surg., Gynec. & Obst. **90**:21-30, 1950.

27. Killins, J. A.: Carcinoma of the Common Bile Duct, Wisconsin M. J. **47**:859-861, 1948.

28. Saypol, G. M., and Fishman, B. S.: Carcinoma of the Extrahepatic Bile Ducts, New York J. Med. **49**:1193-1195, 1949.

29. Pickrell, K. L., and Blalock, A.: The Surgical Treatment of Carcinoma of the Common Bile Duct, Surgery **15**:923-937, 1944.

30. Brunschwig, A., and Bigelow, R. R.: Advanced Carcinoma of the Extrahepatic Bile Ducts: Choleangiocholecystocholedochectomy, Ann. Surg. **122**:522-528, 1945.

extended into the porta hepatis. These cases do not include those previously mentioned and would indicate that the prognosis in cases involving the upper portion of the common duct is about the same as that for the periampullary lesions.

Table 3 summarizes more recent experience with radical pancreaticoduodenectomy for cancers arising in the common duct, though we have not attempted to exhaust the literature on radical pancreaticoduodenectomy for cancers proving to be of common duct origin. Eleven cases, with two operative deaths, are recorded, and five patients have survived 6, 3, 3½, 12, and 19 months, respectively, before dying of their cancers. Two patients reported living and well 7 months and 36 months subsequent to operation and two reported on without clinical details do not constitute an entirely compelling argument against the continuance of local

TABLE 3.—*Radical Pancreaticoduodenectomy for Common Duct Cancer*

	Surgeon, Year	Operation	Lesion	Result
1.	Fallon * 1941	Two-stage pancreaticoduodenectomy	.....	Died 6 mo. postoperatively
2.	Brunschwig and Clark † 1941	One-stage pancreaticoduodenectomy	Anaplastic carcinoma	Died on 2d postoperative day
3.	Brunschwig and Clark †	One-stage pancreaticoduodenectomy with exterior drainage of common duct	Anaplastic carcinoma	Died 3 mo. after first operation and 16 days after second operation, choledochojejunostomy
4.	Pickrell and Blalock [29] 1944	Pancreaticoduodenectomy	Mucus-forming adenocarcinoma of distal common duct	Living and well 7 mo. postoperatively
5.	Dennis and Varco ‡ 1946	Radical pancreaticoduodenectomy	.....	Died of pulmonary embolus on 2d postoperative day
6.	Dennis and Varco ‡	Radical pancreaticoduodenectomy	.....	Living and well after 3½ mo.
7.	Dennis and Varco ‡	Radical pancreaticoduodenectomy	.....	Died 1 yr. postoperatively
8.	Leiter § 1947	Radical pancreaticoduodenectomy	.....	Died 19 mo. postoperatively
9.	Cattell and Pyrtek ‖ 1949	Radical pancreaticoduodenectomy	.....	.....
10.	Cattell and Pyrtek ‖	Radical pancreaticoduodenectomy	.....	.....
11.	Landry ¶ 1950	Pancreaticoduodenectomy	Adenocarcinoma, Grade III	No evidence of disease 3 yr. postoperatively (exploration)

* Reported by Whipple, A. O.: Ann. Surg. **114**:612-615, 1941.
† Surgery **10**:533-562, 1941.
‡ Surgery **20**:72-81, 1946.
§ Surgery **22**:627-647, 1947.
‖ Proc. Staff Meet., Mayo Clin. **25**:179-183, 1950.

excision of "favorable cancers." It is to be remembered that, since many of these cases were reported at the time that the results of local resections were recorded, the more radical procedure has probably been done as a surgical necessity rather than on an elective basis, since the radical procedure was reserved for cases not considered "favorable" for local excision. It is extremely doubtful if the two operations have been used in comparable surgical cases. It is, however, the experience with cancers still recognizable as to their origin and possibly it may be interpreted to perpetuate the paradox of the rare, long-term good results of this limitation in principle as opposed to the sound surgical principles of the radical procedure, which seems to fail as often in durable end-results.

In reviewing the surgical experiences with local excision of cancers arising in the common duct, it is our impression that the local failures or recurrences are

as prominent, but not as readily recognized, as are the occasional startling good results. Review of cases of tumors apparently favorable for local excision reveals that they present the basic characters of the other cancers in this area, that is, they slowly but early infiltrate, though they metastasize late, and an operation which fails to remove the "region of early extension of the tumor" is attended by local recurrence and by present-day standards is not an acceptable operation for cancer. The data at hand indicate that Ransom's statement of this issue in 1938 was prophetic. He stated:

> Assuming that the incidence of carcinoma of the lower common duct or ampulla is somewhat greater than has been generally realized, it is probable that in the future more cases will be found suitable for radical surgery than has been the case heretofore. With the two-stage procedure of Whipple, Parsons and Mullins, the hazard of operation is considerably reduced, while a sufficiently wide margin of tissue is resected to make a permanent cure possible.

This view is in concurrence with the recent summary of Priestley, Walters, Gray, and Waugh,[31] who have concluded that if a neoplasm is situated in the lower end of the duct it is best treated by the Whipple operation, as local excision is almost invariably followed by recurrence.

RADICAL PANCREATODUODENECTOMY FOR RECURRENT CANCERS PRODUCING BILIARY OBSTRUCTION

Child in 1944 presented the case of a 55-year-old woman with symptoms of jaundice of five weeks' duration. At operation in August of 1943 the papilla was explored through a duodenotomy, and a soft adenomatous tumor was found which did not seem to be cancer on either gross or frozen-section examination. Transduodenal excision was done, and the common pancreatic ducts were reimplanted. Approximately six weeks after the operation, the patient was readmitted to the hospital because of jaundice, and on Dec. 20, 1943, two months after the local excision was performed, reexploration showed a firm tumor mass occupying the head of the pancreas, which was resected by a technique which that author has developed. The patient died from metastases 14 months after the operation.

Our present case has been followed only for a six-month postoperative period, not enough time to evaluate the operation's full value, but these six months have been attended with relief of his distress. The silent nature of this recurrence and the attendant long delay in any attempt to cure the patient is further argument against local excision for "favorable cancers." It is to be understood that reoperations for cancer never are as favorable as primary attempts at cure.

An even further extension of this surgical philosophy is that of Brunschwig,[32] who has reported three secondary operations after pancreaticoduodenectomy. One of these was a right colectomy performed for metastasis in the nodes in the base of the mesentery of the ascending colon 20 months after radical resection of the pancreas for ampullary cancer with lymph node metastases. The patient survived this operation four years and ten months.

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31. Priestley, J. T.; Walters, W.; Gray, H. K., and Waugh, J. M.: Annual Report on Surgery of the Biliary System and Pancreas for 1949, Proc. Staff Meet., Mayo Clin. **25**:685-696, 1950.

32. Brunschwig, A.: Reoperation Following Pancreaticoduodenectomy, Cancer **3**:624-628, 1950.

SUMMARY

The surgical philosophy governing local excision of periampullary cancer is reviewed and its failures assessed on the basis of local recurrence. A remarkable case of cancer of the common bile duct resectable by radical pancreatic duodenectomy 51 months after it was locally excised is presented.

The problem of cancer of the lower end of the common bile duct is reviewed, and the resectability of recurrent cancer after local excision by both local procedures and radical pancreaticoduodenectomy is discussed.

The number of secondary resections for recurrent cancer are more prominent than the occasional successful local resection and indicate a failure and limitation of concept of the operation no longer tenable in cancer of the periampullary region.

EFFECTS OF SYMPATHECTOMY ALONE AND COMBINED WITH GASTRECTOMY ON GASTRIC SECRETORY RESPONSES

An Experimental Study on Esophageal-Fistula Dogs with Normal Stomachs

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AND
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SURGICAL procedures which divide the greater splanchnic nerve or its communications with the thoracic ganglions deprive the stomach of its preganglionic sympathetic nerve supply. Neither clinical experience nor experimental studies have disclosed precisely how the sympathetic nerves affect the secretion of gastric juice. Recent reviews of the literature by Shafer and Kittle [1] and by Smithwick and Kneisel [2] reveal considerable disagreement on this subject.

We are not concerned here with the hypothesis that postganglionic sympathectomy potentiates the susceptibility to ulcer [3]; lumbodorsal and transthoracic sympathectomy as commonly employed are preganglionic operations. The concept of antagonism between the two components of the autonomic nervous system as proposed by Hess [4] and by Cannon [5] was originally applied to the motor functions of the gastrointestinal tract. From reports [6] of postsympathectomy ulcer complications which the writers suggest were caused by autonomic imbalance, one concludes that this concept is now being applied to secretory activities.

This paper presents the results of gastric secretory studies made before and after lumbodorsal splanchnicectomy alone and combined with gastrectomy at differ-

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From the Surgical Service and the Smithwick Foundation of the Massachusetts Memorial Hospitals and the Department of Surgery of Boston University School of Medicine.

This paper is No. 3 in a series on a combined clinical and experimental approach to the surgical treatment of peptic ulcer. The first two papers were published in the August, 1951, issue of the ARCHIVES.

1. Shafer, P. W., and Kittle, C. F.: The Relation of the Autonomic Nervous System to Gastric Secretion with Particular Reference to the Sympathetic Nerves, Surgery **29**:1, 1951.

2. Smithwick, R. H., and Kneisel, J. J.: The Effect of Resection of the Sympathetic and Parasympathetic Innervation of the Stomach upon Gastric Acidity, Rev. Gastroenterol. **17**:439, 1950.

3. Lillehei, C. W., and Wangensteen, O. H.: Effect of Celiac Ganglionectomy upon Experimental Ulcer Formation, Proc. Soc. Exper. Biol. & Med. **68**:369, 1948.

4. Hess, J.: Versuche über die peristaltische Bewegung und über die Wirkung der Abführmittel, Deutsches Arch. klin. Med. **40**:93, 1886.

5. Cannon, W. B.: The Wisdom of the Body, New York, W. W. Morton, 1932.

6. Weeks, C.; Ryan, B. J., and Van Hoy, J. M.: Two Deaths Associated with Supradiaphragmatic Vagotomy, Clinical Notes, J. A. M. A. **132**:988 (Dec. 21) 1946. Blegen, H. M., and Kintner, A. R.: Aggravation of a Gastric Ulcer Following Dorsolumbar Sympathectomy, J. A. M. A. **133**:1207 (April 19) 1947. Mason, C., and Pollard, H. M.: Peptic Ulcer Following Splanchnicectomy, Surg., Gynec. & Obst. **89**:271, 1949.

ent levels in esophageal-fistula dogs with normal stomachs and discusses factors which attempt to reconcile some of the opposing conclusions reported in the literature.

METHOD OF STUDY

A detailed report of the method of study employed for animals [7] and for patients [8] in these experiments has already been made. It should suffice here to say that it consists in measuring, in each case before and after surgery, the secretory responses under basal conditions and after broth, insulin and histamine stimulation. This study routine has been adapted to the dog by developing a simple single-stage technique for cervical esophagostomy.[9] By this means the stomach is left in its normal state, and animals can be studied for prolonged periods of time without supplementary feedings or parenteral administration of fluids. A discussion of the interpretation of data collected under the conditions of these experiments has been published.[7] It bears repeating that this method of study is designed, not for collecting absolute physiological data, but for assessing clinically the gastric secretory responses and for indicating the relative changes caused by various surgical procedures. The animals used were group II (mature) dogs according to the classification of Lillehei and Wangensteen.[10] They weighed between 5 and 15 kg. and were, with few exceptions, females.

SYMPATHECTOMY ALONE

Careful studies were made before and after lumbodorsal splanchnicectomy (as described by Smithwick [11]) on five dogs. The sympathetic chain was removed bilaterally from the eighth or ninth dorsal through the first or second, and occasionally through the third, lumbar ganglion. The greater splanchnic nerve was removed from its origin to a point just above the celiac ganglion. The procedure was performed exactly as on human patients except that extrapleural operation was not attempted; also portions of the 12th and 13th rather than the 11th and 12th ribs were removed. The main anatomical difference between the human and the canine subject are that the dog has 13 ribs and thoracic ganglia and an extremely short greater splanchnic nerve originating from the 12th and 13th dorsal ganglia. Operations were performed while the animals were under intravenous pentobarbital sodium anesthesia with intratracheal intubation and positive-pressure oxygen. Blood transfusions and intravenous administration of dextrose and saline were used as indicated. Postoperative studies were begun as soon as the wounds were healed. Postmortem examination on 29 sympathectomized dogs showed that the earliest gross evidence of sympathetic nerve regeneration appeared within three months after operation. We have therefore discarded data obtained more than two months after sympathectomy unless the animal was killed at the conclusion of the experiment and autopsy revealed no evidence of nerve regeneration. The same technique and criteria were used in all the following groups in which sympathectomy was involved.

7. Howe, C. W.; Porell, W. J., and Ware, P. F.: Assessment of Gastric Secretory Responses in Relation to Peptic Ulcer: I. Method of Study and Control Data on 39 Normal Dogs, A. M. A. Arch. Surg. **63**:234 (Aug.) 1951.

8. Farmer, D. A.; Howe, C. W.; Porell, W. J., and Smithwick, R. H.: The Effect of Various Surgical Procedures upon the Acidity of the Gastric Contents of Ulcer Patients, Ann. Surg. **134**:319, 1951. Smithwick and Kneisel.[2]

9. Ware, P. F., and Howe, C. W.: Experimental Esophageal and Pharyngo-Cervical Fistula, A. M. A. Arch. Surg. **63**:229 (Aug.) 1951.

10. Lillehei, C. W., and Wangensteen, O. H.: Effect of Age on Histamine Induced Ulcer in Dogs, Proc. Soc. Exper. Biol. & Med. **68**:129, 1948.

11. Smithwick, R. H.: Technique for Splanchnic Resection for Hypertension, Surgery **7**:1, 1940. Cole, W. H.: Operative Technic in General Surgery, New York Appleton-Century-Crofts Company, Inc., 1950.

Chart 1 shows the preoperative averages of 22 basal, 11 broth and 10 histamine runs and the postoperative averages of 13 basal, 11 broth and 14 histamine runs on five animals. The accompanying table shows the total hour-milliequivalents of acid and per cent reductions. Postoperative insulin-stimulation studies were unsuccessful on many animals because of the extreme insulin hypersensitivity which develops after this procedure consequent to denervation of the adrenal medulla. Among the difficulties encountered with insulin studies were marked convulsive states produced in the sympathectomized animal by small fractions of the preoperative insulin dosage. Dextrose given intravenously would revive these animals, but when the dextrose had to be given before the test was completed, the data could not be used.

Comment.—Chart 1 and the table show that lumbodorsal splanchnicectomy under the conditions of these experiments definitely lowers acidity under basal conditions and after broth and histamine stimulation. The insulin curves in Chart 1 depict the data on the one dog in this group on which a single postoperative test was completed before dextrose had to be given.

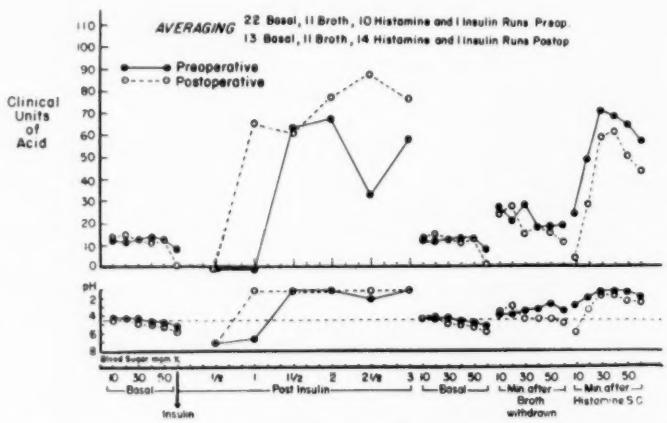

Chart 1.—Composite graph of free acid and pH before and after lumbodorsal sympathectomy in five dogs. Slight postoperative lowering of free acid and elevation of the pH following the basal, broth and histamine runs. (See table for the corresponding reduction in total hour-milliequivalents.) The insulin curves represent tests on one animal only. The preoperative insulin dosage was 8.2 units. The postoperative dose of only 2 units caused hypoglycemic shock, but the run was completed before dextrose had to be given. This graph demonstrates the effect on the secretory responses of the insulin hypersensitivity that develops in dogs after sympathectomy. The same phenomenon occurs in man some time after sympathectomy but only to a slight and probably clinically insignificant degree.

Our attempts to use the Hollander test [12] were hampered by the phenomenon of insulin hypersensitivity first demonstrated by Cannon and his co-workers [13] and con-

12. Hollander, F.: Some Characteristics of Mucous Secretion in the Digestive Tract, Gastroenterology **3**:403, 1944.

13. Cannon, W. B.; McIver, M. A., and Bliss, S. W.: (*a*) The Effect of the Blood Sugar Level on Adrenal Secretion and Sympathetic Activity: A Preliminary Note, Boston M. & S. J. **189**:141, 1923; (*b*) Studies on the Conditions of Activity in Endocrine Glands: XIII. A Sympathetic and Adrenal Mechanism for Mobilizing Sugar in Hypoglycemia, Am. J. Physiol. **69**:46, 1924. (*c*) Dworkin, S.: The Response of Sympathectomized Animals to Insulin, Am. J. Physiol. **98**:467, 1931. (*d*) Brouha, L.; Cannon, W. B., and Dill, D. B.: Blood-Sugar Variations in Normal and in Sympathectomized Dogs, J. Physiol. **95**:431, 1939.

firmed by later investigators. The literature on this subject has been reviewed by Simeone and Vavoudes.[14] In our single successful postoperative insulin test, we observed marked increases not only in volume and in free acid [15] output but also in free acid concentration, compared with the same animal's preoperative insulin responses. These changes are suggestive of heightened vagal stimulation due to the more pronounced hypoglycemia occasioned by increased insulin sensitivity, although changes in arterial inflow may also have contributed.

In man the phenomenon of insulin sensitivity following sympathectomy is far less marked. Simeone and Vavoudes,[14] studying this problem in 29 patients before and after lumbodorsal sympathectomy, concluded that in the immediate postoperative period insulin resistance is increased and the ability to recover from hypoglycemia unimpaired. Later, Simeone and Ramirez,[16] studying insulin tolerance on 26 identical patients approximately one year postoperatively, found the subjects to be more sensitive to insulin and slower to recover from the hypoglycemia induced by it, but

Average Total Millicquivalents of Acid Per Hour Before and After Various Surgical Procedures

Operation	No. of Dogs		Basal	Reduction, %	Broth	Reduction, %	Histamine	Reduction, %	Insulin	Reduction, %
Lumbodorsal splanchnicectomy	5	Before	0.416	....	1.020	....	3.13	....	0.42 *	.....
		After	0.317	23.7	0.800	21.6	2.46	21.4	1.30 *	+118.6
Antrectomy	3	Before	1.11	....	0.94	....	3.46	....	.....	.....
		After	0.505	54.5	0.311	67.0	3.79	+8.5	.....	.....
Lumbodorsal splanchnicectomy plus antrectomy	6	Before	0.265	....	1.010	....	3.580	....	0.511	.....
		After	0.088	66.8	0.084	91.8	2.640	26.2	0.319	37.6
Lumbodorsal splanchnicectomy plus 50% gastrectomy	5	Before	0.435	....	0.825	....	3.470	....	.....	.....
		After	0.213	51.0	0.192	77.0	0.588	83.0	.....	.....
80% gastrectomy	3	Before	0.396	....	0.657	....	3.62	....	0.96 *	.....
		After	0.058	85.4	0.051	92.0	0.145	96.0	0 *	100.0

* One dog only.

far less so than animals. The increase in sensitivity was statistically significant but of doubtful clinical significance, since the late postoperative values show a maximal fall of less than 5% of the fasting level greater than the preoperative fall and insulin-induced hypoglycemia returned to within approximately 5% of the fasting level at the end of three hours. If insulin hypersensitivity has any clinical significance as regards potentiation of the ulcer diathesis, one might expect it to be reflected by an increase in the acidity of the gastric juice during hypoglycemia. This increase has not been observed. It is doubtful whether these slight increases in degree of hypoglycemia could accomplish a significant elevation in the acid levels. Insulin exerts an abnormal potent neurogenic stimulus probably not encountered during the emotional stresses of life.

14. Simeone, F. A., and Vavoudes, H.: The Early Effect of Lumbodorsal Sympathectomy upon the Response to Insulin in Man, Surgery **24**:326, 1948.

15. In this paper the terms acid and free acid refer to values obtained by titrating gastric juice to an end point of around pH 4.5. This titration is well into the buffered acid range and consequently the term free hydrochloric acid is not applicable.

16. Simeone, F. A., and Ramirez, O.: Some Physiologic Effects of Lumbodorsal Sympathectomy for Hypertension, Surgery **28**:282, 1950.

LUMBODORSAL SPLANCHNICECTOMY COMBINED WITH GASTRECTOMY

Gastric secretory studies were carried out before and after lumbodorsal splanchnicectomy combined with antral resection and with 50% gastrectomy. To assess more completely the effects of these procedures, studies were also carried out before and after antrectomy and both 50% and 80% gastrectomy alone.

Estimating the Extent of Resection.—It was at once obvious that the percentage of stomach resected must be measured more accurately. In our experience, x-ray and fluoroscopy studies made shortly after operation indicate that the surgeon's estimate of the extent of gastrectomy is often wrong. Moreover, the roentgenologist himself is sometimes inconsistent in his estimates, which may vary from one examination to another. These discrepancies can probably be explained by such factors as the tonus of the stomach at the time of resection or examination—whether or not the vagi have been divided—and the experience of any given surgeon and roent-

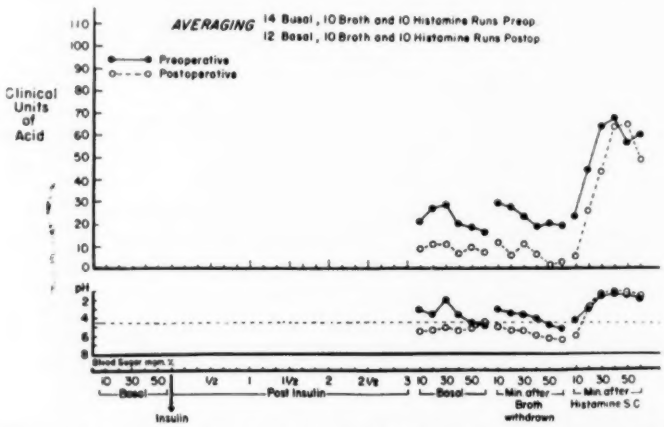

Chart 2.—Composite graph of free acid and pH before and after antrectomy alone in three dogs. Note the postoperative lowering of free acid and elevation of pH in the basal and broth tests, probably due largely to reflux neutralization with alkaline duodenal contents and removal of gastric secretogogues after antrectomy. The acid response to histamine is not significantly reduced, since the majority of the parietal cells remain in the stomach. See table for corresponding data on total hour-milliequivalents.

genologist. This impression was confirmed in our laboratory, where we found that experienced surgeons sometimes erred as much as 10 to 15% (by weight) in their estimates of the amount of stomach resected. We measured, photographed and weighed all specimens and residual stomachs after the animals were killed. Studies on the relationship of stomach weight to total body weight were carried out on 36 other normal dogs. Postmortem examinations of freshly killed animals showed that in dogs weighing between 5 and 15 kg. the mean ratio of stomach weight to total body weight was 0.95% ($S = 0.16$). This information has enabled us to reduce estimating errors by weighing the specimen at the time of operation. If the resection is insufficient, more tissue is removed. If the operation has been too extensive, the animal is classified in a group other than that originally intended. This ratio of stomach weight to total body weight cannot be applied to man; it has been utilized

solely in the experimental animal laboratory as a means of estimating more accurately the amount of residual stomach in the experiments described here.

All gastric resections were Hoffmeister type aseptic procedures performed with the Smithwick clamp.[17] About half of the operations were completed by short proximal afferent loop gastrojejunostomy and the remainder by gastroduodenostomy. No differences were found in the secretory responses in these two groups.

ANTRECTOMY ALONE

In this study we have considered antrectomy to be a resection in which 30% (± 5%) of the stomach, by weight, has been removed. The specimen includes a narrow rim of corrugated gastric mucosa. Gastric secretory studies before and after antrectomy were completed in three dogs. Chart 2 shows the preoperative averages of 14 basal, 10 broth and 10 histamine runs and the postoperative averages of 12

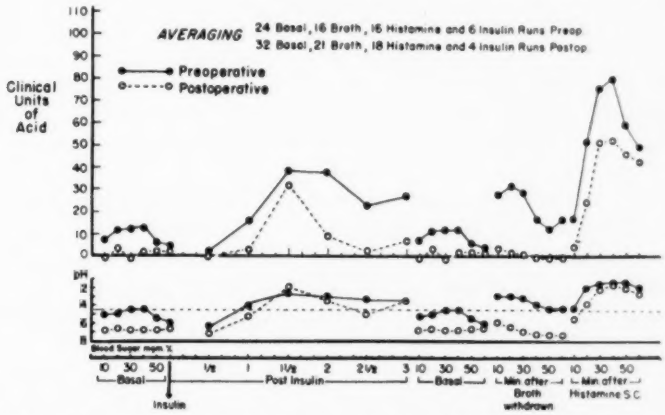

Chart 3.—Composite graph of free acid and pH before and after lumbodorsal splanchnicectomy combined with gastric antral resection in six dogs. The general response to this combined procedure is one of postoperative lowering of acidity in all tests. The pH values are well above the probable level of significant pepsin activation for the basal and broth tests but not for the potent stimuli. The lack of significant pH elevation following insulin stimulation is probably due to the sympathectomy-induced hypersensitivity. Since the parietal cells, which are stimulated directly by histamine, are not removed by this procedure, the pH is raised relatively little during the histamine run. There is more reduction in acid, however, and more pH elevation after the combined procedure than after antrectomy alone.

basal, 10 broth and 10 histamine runs on these animals. Sufficient data were not obtained after insulin stimulation. Total hour-milliequivalents of acid are presented in the table.

Comment.—It can be seen from Chart 2 that antrectomy lowers acidity during basal periods and after broth stimulation but has no effect on histamine response. The lowering during the basal and broth periods might be expected, since antrectomy removes a small amount of acid-secreting tissue and also obliterates the hormonal stimulus.[18] Since the majority of the parietal cells remain, one would anticipate no reduction in acid response to the maximal stimulus of histamine. The absence of

17. Smithwick, R. H.: Total Gastrectomy, New England J. Med. **237**:39, 1947.
18. Edkins, J. S.: The Chemical Mechanism of Gastric Secretion, J. Physiol. **34**:133, 1906.

the buffering effect of the mucus-secreting cells in the antral mucosa might explain the questionably significant increase in the total hour-milliequivalents of acid following histamine shown in the table.

LUMBODORSAL SPLANCHNICECTOMY COMBINED WITH ANTRAL RESECTION

Gastric secretory responses before and after lumbodorsal splanchnicectomy combined with gastric antral resection have been studied in six dogs, including two in the antrectomy group, later sympathectomized and retested. Chart 3 shows the preoperative averages of 24 basal, 16 broth, 16 histamine and 6 insulin runs and the postoperative averages of 32 basal, 21 broth, 18 histamine and 4 insulin runs. Total hour-milliequivalents of acid are reported in the table.

Comment.—All tests, as Chart 3 indicates, show the general effect of the combined procedure to be a lowering of acidity. Interest in this combination was aroused when two patients with known duodenal ulcer underwent lumbodorsal splanchnicectomy and later required emergency surgery (antrectomy) for the control of hemorrhage from a bleeding peptic ulcer. Postoperative studies revealed a surprising "achlorhydria." The data reported by Smithwick and Kneisel [2] on four patients treated with this combination show a 92% reduction in total milliequivalents of acid during basal periods, 80% during insulin, 96% after broth and 76% during histamine stimulation.

The table shows a marked percentage reduction in total milliequivalents per hour of acid in all tests in our dogs. Although considerable, the reductions are still not as great as those in patients except after broth stimulation. The pH values are well above the probable level of significant pepsin activation for the basal and broth tests but not for the potent stimuli. As regards the insulin data, the low pH reflects the hypersensitivity induced by sympathectomy in animals.

Since this procedure does not to any extent remove parietal cells which are stimulated directly by histamine, the pH is elevated relatively little during the postoperative histamine runs. Acidity is more reduced after the combined procedure than after antrectomy alone.

It is of interest that two animals in this group still alive at the end of the fourth and fifth postoperative months, respectively, showed secretory responses to all tests considerably below those within the two-month postoperative period.

LUMBODORSAL SPLANCHNICECTOMY COMBINED WITH 50 PER CENT GASTRIC RESECTION

In conjunction with another experiment, secretory studies were done on a group of eight dogs before and after 50% gastrectomy alone. These were entirely different animals than those used in the experiments described here and, for reasons already stated,[7] cannot be used to evaluate the separate effect that gastric resection contributes to the over-all lowering of the secretory responses in this combined procedure. These data will be presented in a subsequent report on vagectomy combined with gastric resection. It can be said here, however, that 50% gastric resection lowers acidity considerably after all types of stimulation.

Data are available on five animals before and after lumbodorsal splanchnicectomy combined with 50% gastrectomy. Chart 4 is a composite graph of average free acid and pH data obtained from 24 basal, 11 broth and 10 histamine runs pre-

operatively and 24 basal, 16 broth and 17 histamine runs postoperatively; no insulin tests were completed. The table presents total hour-milliequivalents of acid before and after surgery.

Comment.—These data show that lumbodorsal splanchnicectomy combined with 50% gastrectomy markedly lowers acidity under basal conditions and after broth and histamine stimulation. It should be emphasized that variations in the preoperative secretory levels of different animals preclude strict comparison of these data with those for the sympathectomy-antrectomy group.[7] One gets the impression, however, that either combination removes sufficient secretogogues of gastric origin so that no essential difference is noted in basal periods or in response to physiological chemical stimulation. The reduction in response to histamine is, as might be expected, greater with the larger gastric resection by virtue of the removal of more parietal cells. Examination of the data on the 50% resection (alone) group suggests that the gastrectomy component of the combined procedure is responsible

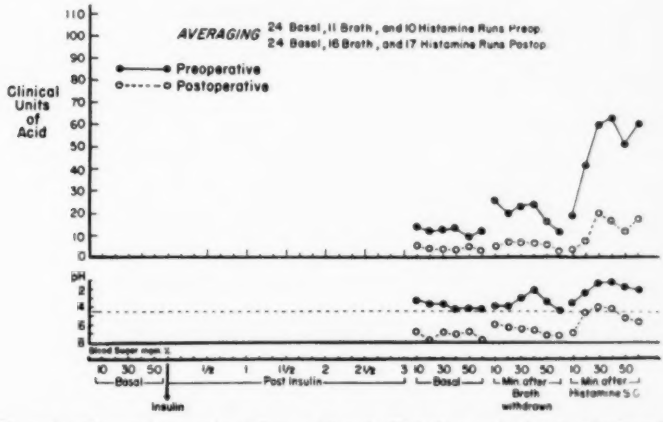

Chart 4.—Composite graph of free acid and pH before and after lumbodorsal splanchnicectomy combined with 50% gastric resection in five dogs. This combined procedure markedly lowers acid values and raises pH under basal conditions and after broth and histamine stimulation. In addition to causing reflex neutralization and removing the gastric secretogogue stimulus, this operation resects some of the parietal cells, so that acid values are greatly reduced after histamine stimulation. These data cannot be compared with those in Chart 3, however, since they were obtained from a different group of dogs.[7]

for most of the observed reduction. These points need further clarification by secretory studies made in the same group of animals after each phase of the various combinations.

EIGHTY PER CENT GASTRIC RESECTION ALONE AND COMBINED WITH LUMBODORSAL SPLANCHNICECTOMY

Since high gastric resection is the most commonly employed surgical maneuver in treating peptic ulcer, it was decided to study its effect on the secretory responses as measured by the methods used in these experiments and to determine how much, when combined with sympathectomy, it contributes to the over-all acid-lowering effect. Chart 5 is a composite graph of free acid and pH before and after 80% gastric resection in three dogs, showing the preoperative averages of 10 basal, 6

broth, 5 histamine and 2 insulin runs and the postoperative averages of 14 basal, 8 broth, 5 histamine and 2 insulin runs. The table depicts the total hour-milliequivalent acid values and the percentage reduction following surgery.

Comment.—The titratable free acidity was reduced postoperatively to zero except for a slight response to histamine and the pH values elevated above the probable level of clinically significant pepsin activation after all types of stimulation.

Examination of the data on these three animals showed reduction in acidity following 80% gastrectomy to be so great that superimposing sympathectomy could not contribute additional titratable acid-lowering effect. One animal was chosen, however, in which some of the postgastrectomy runs showed minimal responses to basal, broth and histamine runs. When lumbodorsal splanchnicectomy was superimposed on the 80% resection in this dog, it was apparent from occasional minimal responses to all tests in some of the postsympathectomy runs that the denervation had contributed no additional lowering effect. The maximal reduction of acidity

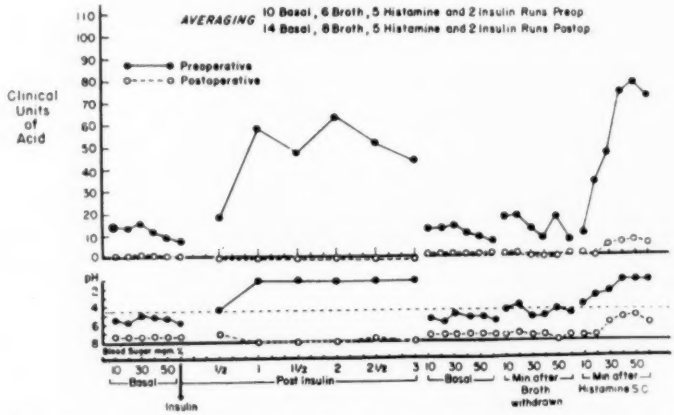

Chart 5.—Composite graph of free acid and pH before and after 80% gastric resection in three dogs. Eighty per cent gastrectomy reduces the measurable units of free acid to zero except for a slight response to histamine stimulation. The pH is elevated above the probable level of pepsin activation after all tests. A superimposed splanchnicectomy does not effect further titratable reduction in acid secretion.

achieved with 80% gastrectomy and the failure of the superimposed sympathectomy to lower acidity further in the dog with minimal responses decided us to abandon the study of this combination of procedures. This animal has been retested with 6 basal, 4 broth, 4 histamine and 2 insulin runs 21 months after gastrectomy and 16 months after sympathectomy. No titratable acid could be demonstrated after any test except histamine, which now stimulates a slight acid response in a few of the 10-minute aliquots.

EFFECTS OF NONSPECIFIC SHAM OPERATIONS

The effects of nonspecific sham operations on secretory responses were studied on two dogs. After preoperative basal, broth, histamine and insulin runs a lumbodorsal incision was made to expose the sympathetic chain without disturbing it. Similar bilateral lumbodorsal incisions were made in a second dog, the peritoneum

opened and the intestines manipulated. Postoperative secretory studies were conducted at the same time-intervals as those used in the previously mentioned experiments. The effect of these procedures was definitely to increase acidity after all types of stimulation except hypoglycemia. The pH was lowered in the basal and broth tests, but the insulin and histamine responses did not change significantly, probably because these potent stimuli produced responses so great as to obscure those brought about surgically.

According to these data, the nonspecific effect of surgery is a general increase in the acid levels, tending therefore to minimize rather than enhance any lowering of acid values specifically produced by our experiments.

POSSIBLE EFFECTS OF BLOOD FLOW ON GASTRIC SECRETION

Vane and Thompson [19] showed that if an increased arterial inflow to the stomach be superimposed on a nearly maximal level of secretory activity, output volume tends to rise and acid concentration to fall. No significant changes are noted at basal levels. Thompson [20] also pointed out that an increase in blood flow will follow bilateral splanchnic-nerve resection providing an adequate blood pressure is maintained.

Shafer and Kittle [1] demonstrated changes in secretory output consistent with increased arterial inflow in their total-pouch dogs. They reported an increased volume and consequently a greater total acidity following sympathectomy. Their data show that the average hydrogen ion concentration actually decreased concurrently with the increased average volume. This effect, they suggest, was due to the fact that the sympathetic nerve impulses normally inhibit gastric secretion. This implies vagal release after sympathectomy. Now, since one would expect pure vagal release to produce a more definite increase in acid concentration as well as in volume, these data suggest to us an increased blood flow effect, because what they actually observed was a slight lowered average acid concentration which probably represents no significant change.

Total-pouch vagally innervated preparations have characteristically high rates of secretory activity even during control periods. One can only speculate as to why total-pouch dogs have such abnormally high secretory levels. The reason may be increased vagal tone because of hypoglycemia mediated by a phenomenon similar to the dumping syndrome in man or by virtue of the animals' admittedly poor nutritional state. Blood sugar determinations during the collection periods would have been of interest in this respect. Intestinal secretogogues may also play a part. Whatever the cause, the control secretory rates were abnormally high at the start of the experiment. Sympathectomy together with daily saline infusions could conceivably result in an increased blood flow sufficient to account for the postoperative increase in secretory level. One cannot eliminate the factor of "vagal release," but the data suggest that the blood flow effect was predominant.

Our data on animals demonstrate a postsympathectomy fall in volume and acidity during the basal and broth-stimulation periods, in neither of which do

19. Vane, J. R., and Thompson, J. E.: Personal communication to the authors. Data to be published.

20. Thompson, J. E.: Personal communication to the authors. Data to be published.

secretory levels rise particularly high. Splanchnicectomy, however, also reduced the average response to histamine although the levels during peaks of the responses were high. The high incidence of postsympathectomy shock in dogs given histamine-in-wax and the rapid thready pulses observed during the histamine tests lead us to believe that histamine-induced hypotension prevented a postsympathectomy increase in gastric blood flow and possibly even decreased it.

It is of interest to note that secretory levels in control total-pouch dogs are approximately within the same range as the basal levels of 41 high-secreting patients with peptic ulcer studied in this clinic [8] whose value for preoperative milliequivalents of free acid per hour was 5.0 and whose average mean pH was 1.8, as compared with 5.4 milliequivalents of acid per hour and an average pH of 1.3 for the total-pouch dogs.

On the other hand, the average basal secretory level in our 39 normal dogs [7] was 0.496 milliequivalents of acid per hour, with an average pH of 4.4. These figures fall within the same ranges as our data on 10 normal human [8] beings, whose average milliequivalents of acid per hour was 0.7 and whose average mean pH was 4.2.

Our baseline secretory levels in dogs with normal intact stomachs [8] resemble more closely data from normal patients without peptic ulcer; the data on Shafer and Kittle's [1] dogs resemble the figures on patients with active peptic ulcer and high secreting levels.

It would seem, therefore, that the crux of the matter is the type of preparation used for study and the level at which the secretory responses are operating in the controls, before sympathectomy is superimposed. This concept helps to reconcile the discrepancies in the literature and in our own conclusions as compared with those of Shafer and Kittle.

CONCLUSIONS

In the early postoperative period, lumbodorsal splanchnicectomy slightly reduces acidity of the gastric juice after physiological neurogenic (basal), physiological chemical (broth) and potent chemical (histamine) stimulation in esophageal-fistula dogs with normal stomachs. Considerable difference exists between hypertensive man and animals as regards potent neurogenic (insulin) stimulation. Sympathectomized animals, in our experiments, show an immediate, marked and persistent increased sensitivity to insulin, which complicates and curtails measurements of acid responses to potent neurogenic stimulation postoperatively. Sympathectomy in hypertensive man as reported by Simeone and others [21] is attended by an increased sensitivity to insulin demonstrable after a preliminary period of increased tolerance. This hypersensitivity is far less than that noted in animals and has not been shown to affect human secretory responses to insulin hypoglycemia or to be of clinical significance.

The response to lumbodorsal splanchnicectomy combined with gastric antral resection in esophageal-fistula dogs with normal stomachs is one of postoperative lowering of acidity following all types of stimulation. The postoperative elevation of pH following insulin stimulation in animals is insignificant by virtue of the hypersensitivity that follows sympathectomy, a phenomenon which occurs to a relatively slight degree in man.

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21. Brouha, Cannon and Dill.[13d] Simeone and Ramirez.[16]

Lumbodorsal splanchnicectomy combined with 50% gastric resection markedly lowers acidity under basal conditions and during broth and histamine stimulation in animals. It appears to be more effective than splanchnicectomy and antrectomy in reducing the acid response to histamine because of the greater number of parietal cells removed.

Eighty per cent gastric resection reduces the titratable free acid to zero after all types of stimulation except histamine, to which there is a slight response. The pH is elevated above the probable level of pepsin activation for all tests.

The addition of lumbodorsal splanchnicectomy to 80% gastric resection appears to effect no further reduction in titratable acidity.

Different types of animal preparations used for the study of gastric secretory responses have wide variations in the level of their baseline secretory responses. A given stimulus may exert different effects on gastric secretory output when applied at varying levels of secretory activity. This appears to be particularly important in regard to the effects of blood flow on the gastric secretions following sympathectomy.

ENDOTRACHEAL CATHETER GUN

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ROCHESTER, N. Y.

WITH THE development of thoracic medicine and surgery in the past decades, the desirability of tracheobronchial catheterization has become ever more frequent. Whereas in the beginning it was seldom used except for the introduction of lipiodal into the tracheobronchial tree, the procedure, in one form or another, can be adapted in a multitude of ways in modern diagnosis and treatment.

One point that is of interest to an endoscopist is the apparent difficulty which many members of the profession have in "getting the catheter into the trachea." Even among endoscopists themselves, the various methods of introduction of such a catheter run a gamut of instrumentation from blind intubation to the use of the more complicated laryngoscopes and bronchoscopes.

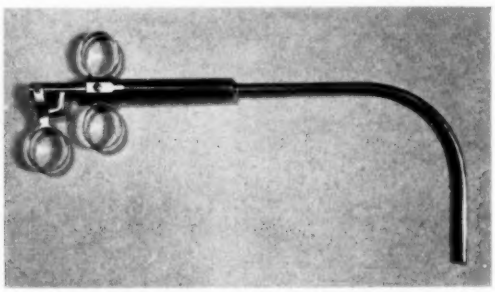

Fig. 1.—The endotracheal catheter gun.

In the hope of bringing some order out of the chaos for the practitioner and of introducing a method which can be used by all with reasonable assurance of success and with a maximum of safety and comfort to the patient, the endotracheal catheter gun has been designed.

THE INSTRUMENT

The endotracheal catheter gun (Fig. 1) is essentially two tubes, one working within the other. The inner tube has incorporated in it a clutch which carries the catheter forward 1½ in. (3.8 cm.) at each application of pressure to the trigger. The outer tube is properly bent to pass over the tongue, hold the epiglottis back out of line of catheter insertion and so bring the catheter directly over the glottic chink.

From the Department of Surgery, Division of Otolaryngology, and in conjunction with the Chest Laboratory of the Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., and in conjunction with the Bronchoscopic Service of the Batavia Veterans Hospital, Batavia, N. Y.

The tubes and clutch have been designed to carry No. 8 through No. 11 French radiopaque ureteral catheters. The reason for choosing these sizes will become apparent when the various uses of the apparatus are discussed.

TECHNIQUE

Catheterization is accomplished with the patient under topical anesthesia, preceded by premedication with morphine, atropine, and pentobarbital sodium in appropriate dosage. Usually the throat is thoroughly sprayed four times with 2% tetracaine (pontocaine®) hydrochloride solution. If this does not completely control the gag reflexes, 2% tetracaine may be used on applicators passed to the deeper reaches of the pyriform sinuses when they are not reached by the spray.

The intratracheal anesthesia is accomplished by dripping the tetracaine directly into the trachea, under direct vision with a laryngeal mirror. For this, 0.5% solution of tetracaine is used, as it allows a satisfactory margin of safety between the necessary volume of solution and possible toxic reactions to the drug.

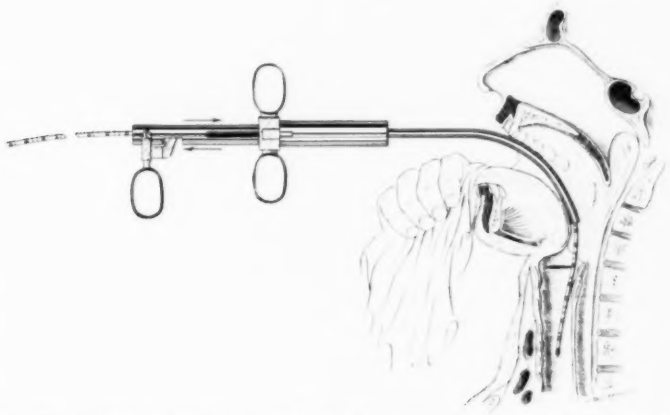

Fig. 2.—The endotracheal catheter gun in position retracting the epiglottis and guiding the catheter on into the trachea.

Once anesthesia has been completed, the technique of actual catheterization is carried out (Fig. 2). Either the patient or an assistant grasps the patient's tongue, pulling it gently forward. The endotracheal catheter gun, containing the catheter of desired size, is then passed over the tongue and, with the aid of a laryngeal mirror, is brought into a position such as to retract the epiglottis and expose the vocal cords and the glottic chink. As the forward end of the gun comes into position over the glottic chink the trigger mechanism is pressed, passing the catheter between the vocal cords on downward into the trachea 1½ in. at a time. The catheter is usually inserted to about the level of the bifurcation, at which time the laryngeal mirror is laid aside, the patient's tongue is allowed to fall back into normal position, and the endotracheal catheter gun withdrawn far enough to allow the operator to grasp the catheter at its forward end.

Thus with the catheter fixed in position, the instrument is back-threaded off the proximal end of the catheter. The catheter is then again advanced to a deeper level, and the patient asked to steady the tube firmly between his lips.

At this point, various adapters can be attached to the catheter, depending on the problem in hand and the patient is transferred to the fluoroscopic table for further insertion of the catheter on into whatever portion of the tracheobronchial tree is under investigation.

COMMENT

The easy introduction of various types of catheters, especially if the catheters be radiopaque and of small circumference, offers to the investigator all manner of possible adaptations of the technique. Probably the commonest use will be, as stated before, the introduction of radiopaque materials into the tracheobronchial tree in the process of making bronchograms. In the experience of the author it has been possible, by using various types of catheters, to obtain bronchograms selectively of any single lobe of the lung or even to place small amounts of radiopaque material into any small selected area within a lobe. This is an advantage in certain surgical problems.

The apparatus lends itself to the treatment of postoperative atelectasis in the absence of a trained bronchoscopist. In such circumstances, with a good source of suction, the technique may well be lifesaving. If carried out under the guidance of the fluoroscope, it has a considerable advantage over blind intubation and suction.

The endotracheal catheter gun and the various types of radiopaque catheters may be used for obtaining cultures from the tracheobronchial tree free of mouth contaminants. Again, as in the making of bronchograms, it allows the investigator to obtain material for culture from the specific regions in question, sometimes with more exactness than the material can be obtained with the bronchoscope.

In a similar manner, the apparatus has been used for obtaining bronchial secretion for cytological examination. While such a procedure is not a substitute for bronchoscopic examination and should not be used as such, it is a comparatively easy means of obtaining additional specimens with a minimum of discomfort to the patient, after the original diagnostic bronchoscopy has been done.

A further use of such apparatus, in conjunction with suitable gas analysis apparatus, is the study of normal pulmonary physiology. Not only does it make it possible to study gaseous exchange and gaseous pressures in the trachea and the main bronchi, but because the smaller catheters can be passed well toward the periphery, small subdivisions can be investigated. Thus, the apparatus may also be used to study pulmonary pathology, both preoperatively and postoperatively.

SUMMARY

An instrument called an endotracheal catheter gun has been introduced. By its design, combined with the use of small-caliber radiopaque catheters, it makes pulmonary catheterization available in an easy and safe form to the members of the profession who are not endoscopists. It has been found satisfactory for the use for which it was designed.

The technique of endotracheal and endobronchial catheterization has been briefly discussed.

Suggestions have been made, and briefly discussed, as to the possible uses to which the instrument and the technique may be put.

The endotracheal catheter gun is available to the profession at the Foregger Company, Inc., 55 West 42nd Street, New York.

TRAUMATIC CHYLOTHORAX

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CHESTER, PA.
AND
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CHYLOTHORAX may be defined as the accumulation of chyle in the pleural cavity. According to Zesas,[1] traumatic chylothorax was first described by Longelot in 1663, but it was not until 1875 that Quincke [2] reported the first authoritative case. The rarity of this condition is brought out by the fact that there are very few cases in the literature. In 1938, Shackelford and Fisher [3] reviewed the literature, discarded 11 cases mentioned too scantily to be included, summarized the remaining 39, and added two cases of their own. In 1947, Lampson [4] reviewed and summarized 17 subsequent reports and added one of his own. We have found seven other cases not included in these two reviews and are adding one case of our own. (There is one case mentioned by Shackelford and Fisher [3]—Heppner's [5]—which is the same case cited by Lampson [4] as Brown's [6] and which therefore is mentioned only once by us, under Heppner's name.) Buxton and Morrison [7] report a case of a perforation of the thoracic duct and the esophagus as the result of a bullet wound, in which the patient vomited chyle. Because of this, chylothorax never developed, but a mediastinal abscess with fistula formation between the thoracic duct and the esophagus was present. This and the vomiting probably prevented the development of chylothorax. The complete list of reported cases is presented in Table 1.

EMBRYOLOGY AND ANATOMY

The adult lymph system results from the budding and fusion of endothelium-lined mesenchymal spaces, all independently of origination of blood vessels. Several

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1. Zesas, D. G.: Die nicht operativ entstandenen Verletzungen des Ductus thoracicus, Deutsche Ztschr. Chir. **115**:49-62, 1912.

2. Quincke, H.: Chyluserguss in serosem hohlem Hydrops chylosus, Deutsche Arch. Klin. Med. **16**:121, 1875.

3. Shackelford, R. T., and Fisher, A. M.: Traumatic Chylothorax, South. M. J. **31**:766-775, 1938.

4. Lampson, R. S.: Traumatic Chylothorax, J. Thoracic Surg. **17**:778-791, 1948.

5. Heppner, G. J.: Bilateral Chylothorax and Chyloperitoneum, J. A. M. A. **102**:1294 (April 21) 1934.

6. Brown, A. L.: Traumatic Rupture of the Thoracic Duct with Bilateral Chylothorax and Chylous Ascites: New Operation; Report of Case, Arch. Surg. **34**:120-124 (Jan.) 1937.

7. Buxton, C. L., and Morrison, D. E.: Gunshot Wound of the Thoracic Duct, U. S. Nav. M. Bull. **46**:1899-1901, 1946.

TABLE 1.—*Cases of Chylothorax Reported in the Literature*

Author*	Date	Age, Sex	Nature of Trauma	Clinical Course	Side†	Therapy	R;	Autopsy Findings
Dienbock	1695	?	Kicked in abdomen by mare	?	?	?	D	Ruptured TD; site unknown
Hoffman [1]	1700	F	Stab wound, left chest	Wasted away, aborted pregnancy	L R	?	D	?
Bonet [1]	?	M	Bullet wound, spine, exit left scapula	Wound seemed minor; 14 days later, chylous effusion; healed, but returned after eating	L	Effusion lasted 28 days; restricted diet	D	No autopsy
Quincke [2]	1875	50 M	Crushed by a wagon	Seemed minor injury; 3d day, effusion	R	Repeated thoracenteses every 2 days; died 21st day	D	7 liters of chyle, right pleura; fractured 7th, 8th, 9th ribs, anteriorly; no hole in TD
Kirchner	1885	9 F	Struck side against wooden sill	Minor injury; 10th day, effusion; occurred just after eating	R	One thoracentesis; fluid recurred but fully absorbed in 2½ mo.; suggested contrecoup	R	.....
Krabbell [1]	1885	16 M	Crushed by a wagon	Effusion on following day; died of asphyxia, 5th day	R ?	None	D	Six liters of chyle; fracture, 9th thoracic vertebra and TD ruptured by bone
von Thaden [1]	1887	31 M	Fall from a mast	5th day, effusion; died on 20th day	R	Thoracenteses on 6th, 11th, 17th days; 7 liters of chyle	D	Fracture of 8th, 9th ribs; 1 liter of chyle on right; hole not found in chest or pleura
Helferich, Port	1894	35 M	Crushed and hyperextended over a cylinder	Minor injury; 4th day, effusion, weight loss; nephritis in 3 wk.	R	Two thoracenteses, then rib resection; 6th day; well in 4 wk.	D	Died of nephritis; no autopsy
Hensen	1897	19 M	Crushed by wagon	Minor injury; bilateral effusion 3 days later	L R	Bilateral thoracenteses; well in 14 days	R	.....
Weisinger	1898	16 M	Crushed by revolving motor spoke	Bilater effusion next day; fracture of clavicle, first 5 ribs, right, and clavicle, left	L	Diagnostic thoracenteses; effusion absorbed in 3 wk; chylothorax, left, hemothorax, right	R	.....
Handmann, Kummell	1899	22 M	Struck in chest by swing	Minor injury; 2 days later, effusion	L	3 thoracenteses	R	.....
Hahn [1]	1899	M	Run over by carriage	Sudden shock, dyspnea on 11th day; wasted away	R	Repeated thoracenteses every 2 days until death, 26th day; 29 liters total	D	Fracture of 9th, 10th ribs, right; 7 liters, right; TD ruptured by callus, 10th rib, right
Legg	1899	62 M	Run over by a cab	Badly hurt; bilateral effusion, next day	L R	None, died 6th day	D	Fracture of 2d left rib, near sternum, 2d right rib near spine, 3d and 4th thoracic vertebrae; rupture of duct not seen
Dietze	1903	39 M	Shot self, left chest	Wound, 6th left interspace; 3 days later, effusion, weight loss	R	8 thoracenteses, 77 liters; 32 lb. weight loss; well in 42 days	R	.....
Newman	1903	36 M	Crushed by a stone	Fracture, left and right clavicles, middle; 4th to 7th ribs, anterior and posterior; effusion, 3d day	L	Repeated thoracenteses—18,600 cc. of chyle; subcutaneous emphysema	R	.....
Lindstrom	1905	18 M	Fell left side, broke rib	Minor injury; fracture, left rib; 4th day, effusion	R	Thoracenteses, then rib resection	D	Ruptured TD at site of fractured left rib, near spine
Haunmesfahr	1907	10 M	Kicked by horse in left sternoclavicular region	Minor injury; bilateral chylothorax, 5th day; well in 8 days	L R	Thoracenteses, 3½ liters on right, 3 liters on left	R	.....
Oeken [4a,b]	1908	20 M	Crushed by stone	Minor injury; 5th day, effusion on right; oliguria, inanition; lived 14 days	R	Intramuscular chyle; repeated thoracenteses, 20 liters	D	6 liters of chyle, right; small opening in right medial pleura found beside, but not into, TD, no bone injury

Slajmer	1912	27 M	Run over by a carriage	Minor injury; 4th day, effusion	L	2 thoracenteses, 2,100 cc. of chyle	R	.....
Bohne-Lowenstein	?	33 M	Fall from a mast	Fracture of ribs and spine, right; died in 2 days	R	None	D	500 cc. of blood, left chest; 1,500 cc. of chyle, right; fracture 10th thoracic vertebra; TD ruptured at this level; fracture 10th to 12th ribs on right at spine
Bohne-Lowenstein	....	21 F	Shot in neck	Immediate dyspnea, fluid; died 5th day	L	Thoracenteses on 1st and 5th days, 2,100 and 1,900 cc.	D	1,300 cc. of chyle on left; at apex of left lung, perforation of pleura and TD severed at junction with vein
Derganz	1915	20 M	Gunshot, right sterno-clavicular area and exit on left, spine and scapula	Next day, fluid and air in left chest; 11th day, sudden dyspnea, marked thirst; well in 2 mo.	L	Thoracenteses; rib resection 30th day; fluid mistaken for empyema	R	.....
Pisek	1917	9 wk. F	Convulsion, respiratory difficulty	Right effusion, 10 days after convulsion; well in 27 days	R	Repeated thoracenteses	R	.....
Elliott and Henry	1917	M	Shrapnel wound, right clavicle, left anterior axilla	Walked 1 mile after injury; 4th day, empyema, effusion on left; well in 10 days	L	Thoracenteses; rib resection, 8th day	R	.....
Elliott and Henry	1917	M	Bullet wound, throat, below thyroid	Minor injury; 4th day, chylothorax; died 11th day, perfringens infection	L	Thoracenteses; rib resection, 5th day	D	Bullet wound trachea, below the cricoid; exit on left, through apex of pleura; actual hole in duct not found; clotted chyle in chest
Malone and Wardrup	1919	22 M	Fall from a mast	Minor injury, not treated; 10 days later, dyspnea, emaciation; died in 24 days	R	12 thoracenteses totaling 48,840 cc.	D	No injury to TD found; pleural thickening
Lindenfeld	1919	..	Struck on right chest	Cylothorax 3 wk. later	R	Thoracenteses	R	.....
Watts	1921	35 M	Stab wound, suprasternal notch	Chylothorax next day with inanition, thirst, anemia; died in 3 wk.	L R	Thoracenteses	D	Left pleura and TD severed; chyle in both sides of chest
Lindenberg	1926	33 M	Crushed between 2 wagons	4th day, dyspnea, oliguria; well in 5 wk.	L R	Repeated thoracenteses totaling 10.6 liters; left stopped first	R	.....
Grimault	1928	36 M	Struck by automobile after full meal	Operation, fractured skull; 6 wk. later, chylothorax; well in 5 mo.	R	3 thoracenteses totaling 12 liters	R	.....
Spaciabello	1928	18 M	Left neck punctured by carriage shaft	Next day emphysema and left chylothorax; drained 900 cc. per day; well in 5 mo.	L	Repeated thoracenteses until infected, then rib resection	R	.....
Marchet	1930	F	Automobile accident; chest against front seat	Fracture 8-9 ribs, left; 14 days later, chylothorax, sudden dyspnea, oliguria, thirst, emaciation	L	22 thoracenteses, to total of 37 liters; oxygen, paraffin injected in vein; rib resection in 12 days	D	No autopsy
Andrews	1929	52 M	Crushed by automobile	7 days later sudden dyspnea, etc.; methylene blue by mouth appeared in chest; died in 15 days	R	.....	D	3 liters in right chest and small amount in pericardium; TD perforated by broken arthritic spur
Paitre [38]	1929	M	Struck by automobile before eating	Two days later, sudden shock; right rib broken in posterior axillary line; well in 10 days	L	Thoracenteses, 300 cc.; diet—sugar, champagne, rectal feedings	R	.....
McNab and Scarlett [35]	1932	46 M	Fell, landed on back	Minor injury; 6 days later sudden shock; died in 2 mo.	R	Daily thoracenteses, total of 35 liters in 48 days; thoracotomy on 50th day	D	Rupture of thoracic duct at T 10 and connected with mediastinal chyloma
Scott	1934	37 M	Crushed by truck	Immediate intraperitoneal hemorrhage; 19 days later, sudden chylothorax, right; well in 63 days	R	Immediate thoracotomy; nothing by mouth	R	.....

TABLE 1.—*Cases of Chylothorax Reported in the Literature—Continued*

Author*	Date	Age, Sex	Nature of Trauma	Clinical Course	Side†	Therapy	R‡	Autopsy Findings
Heppner [5]	1934	19 F	Thrown against front automobile seat	Fractured forearm; open reduction 3 wk. later; 5 wk. later, sudden dyspnea; 9 wk. later, ascites; died in 16 wk., one day after posterior mediastinotomy	L R A	Repeated thoracenteses; fed chyle; laparotomy after ascites; posterior mediastinotomy	D	Rupture TD 2 to 5 cm. above diaphragm; bilateral chylothorax and ascites; bilateral adrenal hemorrhage
Lillie and Fox	1935	45 M	Fell from a scaffold	Fractured T 11, T 12, 10th and 11th ribs, 1½ in. from spine; fracture, right olecranon; concussion; 5th day, sudden shock; 34 lb. weight loss; well in 6 mo.	R	Repeated thoracenteses, total of 52,750 cc.; fat-free diet which seemed to decrease flow from 4 liters to 250 cc. in 48 hr.; intravenous fluids; no taps after 5 wk.	R	.....
Shackelford and Fisher [3]	1930	45 F	Fell 18 ft. on back	Minor injury, sent home; 1 mo. later gradual chylothorax and ascites; fracture, 1st lumbar vertebra; well in 3 mo.	R A	Repeated thoracenteses and paracenteses	R	.....
Shackelford and Fisher [3]	1935	20 F	Thrown against steering wheel	Minor injury, dislocated hip, reduced; 18 hr. later, sudden shock; well in 16 mo.	R	Repeated thoracenteses and paracenteses	R	.....
Bauersfeld [44a]	1937	22 M	Automobile accident	Serious injury; 8 days later, massive effusion; lost weight	R	Repeated thoracenteses—22,275 cc. of chyle; 1,000 cc. and 200 cc. given intravenously	R	.....
Bravo and Huertas	1935	39 M	Train wreck—hyperextension of spine	Chylous effusion on 2d day	R	1 diagnostic thoracenteses	?	Chylous effusion still present when Shackelford and Fisher reported this in 1938
Strauss [39]	1936	24 F	Bullet wound, chest	10 days later, shock, dyspnea, chylothorax; well in 3 mo.	R	Repeated thoracenteses and pneumothorax; 36 taps—79,800 cc.	R	.....
Douday, Dupuy, and Bouvrain	1938	39 M	Lysis of adhesions of left lung by thoracoscope for tuberculosis	Fever, dyspnea, chyle in chest on first day	L	7 days later, 100 cc. of milky fluid removed; recovery, 15 days	R	.....
Fujita, Bando, and Sugishita	1939	10 M	Struck in left infraclavicular area; fractures	Fracture, left 1st rib; left chylothorax	L	Repeated taps; incision, left neck and cervical thoracic duct; compressed with pack; well in 3 mo.	R	.....
Everhart and Jacobs	1939	15 days F	Vigorous resuscitation at birth	Cyanotic, resuscitative measures; x-ray, fluid right chest; dyspnea, cyanosis, weight loss, death on 21st day	R	Repeated taps, weight loss, tap every 24-36 hr.—50-100 cc. of chyle	D	Leak of chyle in posterior mediastinum, 1½ in. above diaphragm; TD not found
Gordon	1940	31 M	Blow on chest	1 mo. later, cough, milky fluid on tap; bed rest, 7 mo.; hospitalized 4 mo., tap once a month	R	Repeated taps for 3 mo.; chest irrigation for 3 mo. with chloroazodin, 1-3,300; fluid diminished	R	.....
Cellan-Jones and Murphy [16]	1940	32 M	Blow and crush of chest at mid-back; abrasion, back; questionable injury to 9th thoracic vertebra	Dyspnea, collapse 3 days later; died 15 days after injury	R	Repeated taps—27 pt. (13 liters) in 12 days	D	Fracture T 9, T 10; TD torn as well as parietal pleura communicating with right side of chest
Matson and Stacy	1940	21 M	Gunshot wound, right chest	Shock, pneumohemothorax, repeated taps, chyle noted on 12th day	R	Repeated taps—22,440 cc.; cajuput oil injected; well in 5 mo.	R	.....
Hoyer	1941	56 M	Hit by automobile; fracture, 9 to 11 ribs, right; chylothorax 5 days later; well in 40 days	Chylothorax 5 days later; well in 40 days	R	Repeated taps—total, 6,600 cc.	R	.....

Baldridge and Lewis [26]	1941	35 F	Surgical injury during sympathectomy	Collapse, shock on 10th postoperative day	R	Repeated taps—32,180 cc. aspirated from 10th to 45th postoperative days; high calory, protein, carbohydrate diet; phrenic neurotripsy on 33d postoperative day; intravenous "amigen," plasma, blood; reoperation on 34th postoperative day; rent in cisterna chyli repaired	R	.....
Smith and Wolfver [29]	1941	17 F	Surgical accident	TD injured and not ligated during a resection of a tumor of the 10th rib and vertebra; dyspnea on 3d postoperative day; well on 15th postoperative day	R	Repeated taps—total of 8,700 cc. from 5th to 12th postoperative days; 3,000 cc. given; well, with spontaneous closure on 15th postoperative day	R	.....
Dorsey and Morris [31]	1942	60 M	Fall	Fractured 10th rib; dyspnea 28 days later; tap—3,100 cc. of milky fluid; died 46 days after injury	R	Repeated taps—18,400 cc. in 18 days; pneumothorax; 3,500 cc. of chyle intravenously	D	TD had opening over 12th thoracic vertebra; fracture of 9th and 10th ribs
Little, Harrison, and Blalock	1942	17 F	Automobile accident	Dyspnea 7 wk. later; chyle in left and right sides of chest and peritoneal cavity	L R A	Repeated taps, chest and abdomen; 11,100 cc. of chyle intravenously; over 500 liters from taps; finally died	D	No autopsy
Whitcomb and Scoville [32a]	1942	39 F	Surgical accident; TD injured, recognized, and clipped during right sympathectomy	14th postoperative day, severe dyspnea; died in anaphylactic shock during injection of chyle	R	Repeated taps; slow intravenous injection of chyle; shock and death after 75 cc.	D	No autopsy
Schnug and Ransohoff [40]	1943	23 M	Bullet wound, 5th interspace, right; bullet in left posterior T 11; hemoperitoneum clinically	Immediate laparotomy; 6 days later, dyspnea; tapped, chyle in right chest	R	Repeated taps—56,450 cc. over 33 days; right phrenic crush 15th day; intravenous chyle—16,800 cc.; on 32d day, 50 cc. of sterile broth injected into right chest; chyle stopped on 33d day	R	.....
Peet and Campbell	1943	47 M	Surgical accident, bilateral splanchnicectomy	11 days later, sudden collapse and dyspnea; chylothorax	R	Three taps in 5 days—10,700 cc.; chyle intravenously and intrasternally; operative ligature attempted, done, patient died suddenly on table	D	TD interrupted at T 11; no satisfactory cause of death found
Traquair	1944	23 M	Kicked in epigastrium, played football for a few minutes, collapsed; bed rest, pain, anorexia, shoulder pain; admitted 2 wk. after injury	Pancreatic cyst and bile peritonitis; 15 wk. after admission, left chylothorax	L	Repeated taps 7 times, every 10 days, 180 to 500 cc. each time; sterile; less each time; 5 mo. after admission, chylous ascites after subphrenic abscess; wound infection; operations—pancreatic cyst, bile peritonitis, subphrenic abscess	R	.....
Buxton and Morrison [7]	1945	28 M	Bullet wound, right anterior chest to left costovertebral angle; fracture of 5th and 6th ribs; 1,200 cc. of air and 250 cc. of blood in left chest; fracture, left scapula	Nausea, vomiting, diarrhea, dehydration; 5 wk. after injury, thin pale fluid on taps; vomited chylous material; death on 43d day	L	1 thoracentesis, 1 paracentesis; emetine	D	Adhesions, right and left pleural cavities; fracture, 5th, 6th ribs and scapula, left lateral aspect of T 4, with overlying abscess communicating with TD and esophagus; 2 perforations of esophagus and 1 of TD

TABLE 1.—*Cases of Chylothorax Reported in the Literature—Continued*

Author*	Date	Age, Sex	Nature of Trauma	Clinical Course	Side†	Therapy	R‡	Autopsy Findings
Florer and Ochsner [42]	1945	14 M	Fall	4 days later, dyspnea; tap, right, 1,100 cc.	R	16 taps—2,000 cc.; right phrenic nerve crushed; intravenous chyle; fat-free diet; died 24 days after injury	D	Perforated duodenal ulcer; TD narrowed 3 cm. above cisterna chyli; small rent in pleura at 11th interspace; no fractures
Loe	1946	M	Bullet wound of neck	Shock, respiratory distress	L	Repeated taps—1,800 cc. in 9 days; chyle on 4th day; on 9th day, duct ligated in neck	R	.....
Lampson [4]	1946	35 F	Paroxysms of coughing 2 mo. before (pneumonia)	Chylothorax 2½ mo. later, dyspnea; diagnostic tap	L	Repeated taps; pneumothorax; diet low in fluids, protein and fat; left thoracotomy—ligation of duct	R	.....
Berry	1947	28 M	Shrapnel wound, left chest	Foreign body removed from left chest; thoracotomy; 48 hr. later, dyspnea; tap—800 cc. bloody chyle	L	Repeated taps, 8 days; cure 14th day; 10,375 cc.	R	.....
Whiteside, Stewart, and Cuthbertson [50]	1947	30 M	Gunshot wound, right side of chest	Pain, dyspnea, hemothorax; chyle; first recognized on 8th day	R	Repeated taps—21,065 cc. plasma; downhill course; thoracotomy, 19th day, ligation of TD, sodium morrhuate injection, fibrin foam application	R	.....
Whiteside [50]	1947	10 F	Surgical injury during tetralogy of Fallot operation	Chylothorax on 3d postoperative day	L	Repeated taps—over 12,000 cc.; no benefit; reoperation—ligated as in case 64, about 2 wk. after 1st operation	R	.....
Authors' case								

* Dienbock, cited by Zesas [1] and by McNab and Scarlett.[35] Kirchner: Ein Fall von rechtsseitigem Chylothorax in Folge von Ruptur des Ductus thoracicus, nebst Statistik und Kritik der bisher bekannten einschlogigen, Fälle, Arch. Klin. Chir. **32**:156-181, 1885, cited by Shackelford and Fisher.[3] Port, K.: Traumatic Chylothorax, Deutsche Ztschr. Chir. **39**:572, 1894; cited by Shackelford and Fisher.[3] Handmann: Two Cases of Chylothorax, München. med. Wchnschr. **46**:181, 1899; cited by Shackelford and Fisher.[3] Weisinger, cited by Mouchet, A.: Traumatic Chylothorax with Report of a Case, J. Chir. **42**:386-399, 1933. Lezg, T. P.: Case of Bilateral Chylothorax Following Injury, St. Barth. Hosp. J. **6**:163, 1898, 1899; cited by Shackelford and Fisher.[3] Dietze, cited by Shackelford and Fisher.[3] Newman, D.: Chylothorax from Rupture of the Thoracic or of One of the Large Lymphatic Ducts, Glasgow M. J. **59**:117-121, 1903; cited by Shackelford and Fisher.[3] Lindstrom, cited by Shackelford and Fisher.[3] Hammestahr, A.: A Case of Bilateral Chylothorax, München. med. Wchnschr. **54**:1876, 1907; cited by Shackelford and Fisher.[3] Slajmer, cited by Shackelford and Fisher.[3] Bohne-Lowenstein, cited by Shackelford and Fisher.[3] Derganz, F.: Chylothorax traumaticus, Wien. Klin. Wchnschr. **28**:1320, 1915; cited by Shackelford and Fisher.[3] Pisek, G. R.: A Case of Chylothorax, Arch. Pediat. **34**:929, 1917. Elliott, T. R., and Henry, H.: Chylohaemothorax from Wounds Involving the Thoracic Duct, Lancet **1**:872-874, 1917. Malone, A. E., and Wardrup, J. G.: Recurrent Chylothorax Following Trauma, Lancet **1**:1116, 1919. Lindenfeld, cited by Mouchet. Watts, S. H.: Traumatic Chylothorax, Ann. Surg. **74**:691, 1921. Lindenberg, F.: Bilateral Traumatic Chylothorax, München. med. Wchnschr. **54**:1876, 1907. Grimault: Traumatic Chylothorax, Bull. et mem. Soc. Nat. de chir. **54**:172-179, 1928. Spaciabello, cited by Mouchet. Marchet, cited by Mouchet. Andres, C. F.: Traumatic Intrathoracic Rupture of Thoracic Duct with Chylothorax, Nebraska M. J. **14**:26-295, 1929. Scott, J. F.: Rupture of the Thoracic Duct, Northwest Med. **33**:50-51, 1934. Lillie, O. R., and Fox, G. W.: Traumatic Rupture of the Intrathoracic Duct with Chylothorax, Ann. Surg. **101**:1367-1376, 1935. Bravo, J., and Huertas, A.: Quilotórax traumático Med. ibera **1**:379-382, 1935; cited by Shackelford and Fisher.[3] Douday, D.; Dupuy, D., and Bouvrain, Y.: Chylothorax benin après section d'adhérences pleurales, Arch. Med. chir. de l'opp respir. **13**:284-291, 1938. Fujita, K., Bando, T., and Sugishita, J.: Ein Fall von Chylothorax traumaticus, Arch. jap. chir. **16**:226-237, 1939; cited in Lampson.[4] Gordon, J.: Traumatic Chylothorax, Ann. Int. Med. **13**:1998-2004, 1940; personal communication to Lampson.[4] Matson, R. C., and Stacy, J. W.: Traumatic Chylothorax, Dis. Chest **6**:332-336, 1940. Hoyer, A.: Chylotoraks, Nord. med. tidskr. **9**:40-44, 1941, cited by Lampson.[4] Everhart, J. K., and Jacobs, A. H.: Chylothorax, J. Pediat. **15**:558-562, 1939. Blalock, A.: Personal communication to Lampson.[4] Little, Harrison and Blalock.[32b] Peet, M. M., and Campbell, K. N.: Massive Chylothorax Following Splanchnicectomy Treatment with Intravenous and Intrasternal Transfusions of Chyle, University Hosp. Bull., Ann Arbor, **9**:2-3, 1943. Traquair, K.: Chylothorax Following Traumatic Pseudocyst of the Pancreas, Brit. J. Surg. **33**:297, 1946. Loe, R. H.: Injuries of the Thoracic Duct: Report of a Case of Chylothorax in Which the Patient Recovered after Ligation of the Thoracic Duct, Arch. Surg. **53**:448-455 (Oct.) 1946. Berry, W. H.: Traumatic Chylothorax Resulting from Battle Injury, J. A. M. A. **133**:319-320 (Feb. 1) 1947.

† R indicates right side of chest; L, left side of chest, and A, abdomen.

‡ Under result (R), D signifies death and R recovery.

§ TD indicates thoracic duct.

lymph sacs develop with openings into veins, the right lymphatic duct and the left thoracic duct. Another lymph sac develops ventral to the body of the second lumbar vertebra, the cisterna chyli. Embryonically, the thoracic ducts are bilateral, with cross anastomoses. Lee [8] was of the opinion that it is the persistence of these cross anastomoses that is important in the development of collateral circulation after injury to, or obstruction of, the duct. He found that many of these small collaterals communicate by small filaments with the lumbar, intercostal and azygos veins. He suggested that there are lymphaticovenous anastomoses in the peritoneal cavity. He found that a fairly extensive collateral circulation becomes established between seven and eight days after ligation of the thoracic duct. Blalock and others [9] ligated the superior vena cava in dogs and cats and found that chylothorax developed in approximately one-half of the animals. They state that the fact that occlusion of the right and left thoracic ducts does not produce chylothorax indicates that there are a number of other lymph vessels that empty into the superior vena cava or its branches.

Van Pernis [10] has reviewed the anatomy of the thoracic duct in a study of 1,081 dissections. The length of the duct from the receptaculum chyli to the subclavian vein ranged from 36 to 45 cm. He found that the upper boundary of the cisterna chyli was at the level of the second lumbar vertebra in 56% of the cases, at the level of the first lumbar vertebra in 33%, and at the level of the 12th thoracic vertebra in 10%. The tributary trunks of the cisterna chyli are (1) the bilateral lumbar, (2) the bilateral intestinal, and (3) the bilateral descending trunks, draining the lymph from the lower six or seven thoracic interspaces. The right thoracic duct, according to Gray's "Anatomy of the Human Body,"[11] measures approximately 1.25 cm. in length and normally ends in the right subclavian veins at its junction with the right internal jugular vein. This duct drains the right lobe of the liver, the right lung, the right side of the heart, the right side of the thorax, the right upper extremity, and the right side of the head and neck. Lymph from the rest of the body and lymph from the intestine are drained by the main thoracic duct. This shall be referred to as the thoracic duct. Van Pernis [10] found that the thoracic duct always passed through the aortic hiatus between the aorta and the azygos vein. In the aortic hiatus the thoracic duct and splanchnic nerves are very close to each other. Low in the right chest the duct may lie directly against the azygos vein and the great splanchnic nerve may lie directly over the vein. The site of crossing of the main duct from right to left was at the level of the sixth thoracic vertebra in 56% of the cases and at the level of the fifth in 44%. The thoracic duct enters the superior mediastinum, on the left, and ascends behind the aortic arch and the subclavian artery, between the left side of the esophagus and the left parietal pleura to the upper orifice of the thorax. Van Pernis [10] found that 61% of his cases showed single ducts, varying in diameter from 2 to 4 mm., and 39% showed two or more branches of variable length. From the upper orifice of the thorax the main thoracic duct arched 3 to 5 cm. above the left clavicle, crossing

8. Lee, F. C.: The Establishment of Collateral Circulation Following Ligation of the Thoracic Duct, Bull. Johns Hopkins Hosp. **33**:21-31, 1922.

9. Blalock, A.; Cunningham, R. S., and Robinson, C. S.: Experimental Production of Chylothorax by Occlusion of the Superior Vena Cava, Ann. Surg. **104**:359, 1936.

10. Van Pernis, P. A.: Variations of the Thoracic Duct, Surgery **26**:806-809, 1949.

11. Gray, H.: Anatomy of the Human Body, ed. 25, Philadelphia, Lea & Febiger, 1948.

anterior to the subclavian artery in 92% of the cases and posteriorly in the rest. The duct was always anterior to the vertebral artery and vein and the thyrocervical trunk, lying in front of the phrenic nerve and medial to the scalenus anticus muscle. It ended in the angle, or within 1 cm. of the angle, formed by the junction of the left subclavian and left internal jugular veins. There was only one constant valve in the thoracic duct, a terminal valve in the last 1 cm. of the duct. Acevedo [12] found that the wall of the thoracic duct contained smooth muscle fibers.

PHYSIOLOGY

The liver and the intestines contribute 95% of the volume of the thoracic duct lymph.[13] Intestinal lymph becomes chylous in the fat-fed animal, indicating its role in the absorption and transport of neutral fats, fatty acids and esters.[14] Sixty to 70% of ingested fat passes along the thoracic duct in the chyle. The protein content of chyle ranges from 1 to 6 gm. per 100 cc. and is thought to aid in the emulsification of fat.[15] The loss of such a protein and fat-rich food produces inanition and dehydration.

The flow through the thoracic duct to the veins of the neck ranges between 50 and 195 cc. of chyle per hour, at a rate of 4 mm. per second. The pulsations of the adjacent arteries may be an important factor in producing lymph pressure. The latter is less than the venous pressure, and, according to Cellan-Jones and Murphy,[16] is raised by the intravenous administration of dextrose. Beck [17] found a rise in lymph pressure when certain lymphagogues were injected into the blood stream, i. e., hypertonic or isotonic sodium chloride solution, dextrose, histamine, epinephrine, and peptones. Acevedo [12] feels that rhythmic contractions of the smooth muscle fibers in the wall of the thoracic duct help propel the chyle upward along the duct. The changes in intrathoracic pressure with respiration and the accumulation of chyle in the cisterna chyli are also important factors in its flow. Judd and Nix [13] mention muscular activity, intestinal peristalsis, and changes in intra-abdominal pressure as additional forces influential in the transport of lymph.

The rate of lymph flow varies directly with age,[18] size,[18] degree of hydration,[19] exercise,[20] digestion of food,[20a] ingestion of water,[19] degree of anoxemia,[21] and

12. Acevedo, D.: Motor Control of the Thoracic Duct, Am. J. Physiol. **139**:600-603, 1943.

13. Judd, E. S. Jr., and Nix, J. T.: Spontaneous and Traumatic Lymph Fistulas: Data on 40 Cases, S. Clin. North America **29**:1035-1045, 1949.

14. Munk, I., and Rosenstein, A.: Zur Lehre von der Resorption im Darm, nach Untersuchungen und einer Lymph-(Chylus-)fistel beim Menschen, Arch. path. Anat. **123**:484-518, 1891.

15. Drinker, C. K.: Extravascular Protein and Lymphatic System, Ann. New York Acad. Sc. **46**:807-821, 1946.

16. Cellan-Jones, C. J., and Murphy, N.: Traumatic Chylothorax, Brit. M. J. **2**:590-591, 1940.

17. Beck, C. S.: A Study of Lymph Pressure, Bull. Johns Hopkins Hosp. **35**:206, 1924.

18. Drinker, C. K., and Yoffey, J. M.: Lymphatics, Lymph and Lymphoid Tissue: Their Physiological and Clinical Significance, Cambridge, Mass., Harvard University Press, 1941, pp. 406.

19. Straling, E. H.: The Influence of Mechanical Factors on Lymph Production, J. Physiol. **16**:224-267, 1894.

20. (*a*) Crandall, L. A. Jr.; Barker, S. B., and Graham, D. G.: A Study of the Lymph Flow from a Patient with Thoracic Duct Fistula, Gastroenterology **1**:1040-1048, 1943. (*b*) Drinker and Yoffey.[18]

21. Maurer, F. W.: The Effects of Decreased Blood Oxygen and Increased Blood Carbon Dioxide on the Flow and Composition of Cervical and Cardiac Lymph, Am. J. Physiol. **131**:331-348, 1940.

presence of anaphylactic shock,[22] increasing with the increase of each of these factors. The rate of flow decreases in direct proportion to the degree of hypoproteinemia,[19] anemia,[19] and hemorrhage.[23] With the use of local infiltration of procaine as a baseline, it has been found that the lymph flow increases with ether anesthesia but decreases with barbiturate anesthesia.[24] Acevedo[12] canalized the cisterna chyli and the thoracic duct, experimentally, and found that acetylcholine and vagal stimulation produced constriction of the ducts and that epinephrine produced a dilatation.

The main characteristics of chyle according to Nowak and Barton,[25] Gaudin,[26] and Wallis and Scholberg[27] are listed by Jahsman[28] as the following: (1) milky appearance, (2) creamy layer on standing, (3) finely emulsified, with fine fat globules, (4) no odor, or an odor corresponding to that of food eaten, (5) alkaline reaction, (6) specific gravity exceeding 1.012, (7) constant degree of opalescence, (8) sterile and resisting putrefaction, (9) fat content generally high, 0.4 to 4%, and like fat in food, (10) total solids usually greater than 4%, (11) total protein generally exceeding 3 gm. per 100 cc., ranging from 1 to 6 gm., (12) salts and organic substances approximating the values found for chyle from the thoracic duct, and (13) fat droplets microscopically. In addition to the above, the fat droplets take the Sudan III stain. Smith and Woliver[29] state that the chyle in their case contained relatively few red blood cells and leucocytes, 90% of the latter being lymphocytes. Hodge and Bridges[30] point out that the nonprotein nitrogen, sugar, urea, and minerals are similar in amount to those found in the blood stream. The calcium and cholesterol contents are slightly lower than those of the blood. The lymphocyte and eosinophile counts are much higher than in the blood, where they are reduced. Blalock and others[9] found that in fatal experimental chylothorax there is a decrease in the number of lymphocytes and a disappearance of the eosinophiles in the chest fluid. Uric acid, phosphatase, phosphorus, sodium, potassium, magnesium, water, and solids are present in chyle, but there is very little fibrinogen.

There is strong indication[31] that within 24 hours of the establishment of chylothorax the blood fat levels are diminished by approximately 25% of normal values

22. McCarrell, J. D., and Drinker, C. K.: Cervical Lymph Production During Histamine Shock in the Dog, Am. J. Physiol. **133**:64-69, 1941.

23. Haynes, F. W.: Factors Which Influence the Flow and Protein Content of Subcutaneous Lymph in the Dog: I. Hemorrhage and Hyperemia, Am. J. Physiol. **101**:223-231, 1932.

24. Polderman, H.; McCarrell, J. D., and Beecher, H. H.: Effect of Anesthesia on Lymph Flow, J. Pharmacol. & Exper. Therap. **78**:400-406, 1943.

25. Nowak, S. J. G., and Barton, P. N.: Chylothorax: Report of Case Arrested by Phrenicotomy, J. Thoracic Surg. **10**:628, 1941.

26. Gaudin, S.: Pathogenese und Klassifikation der milchartigen Ergüsse, Ergebn. inn. Med. u. Kinderh. **12**:218, 1913.

27. Wallis, R. L., and Scholberg, H. A.: On Chylous and Pseudochylous Ascites, Quart. J. Med. **3**:301, 1910.

28. Jahsman, W. E.: Chylothorax: Brief Review of Literature; Report of 3 Non-Traumatic Cases, Ann. Int. Med. **21**:669-678, 1944.

29. Smith, D. D., and Woliver, E. M.: Traumatic Chylothorax, Arch. Surg. **43**:627-632 (Oct.) 1941.

30. Hodge, G. B., and Bridges, H.: Surgical Management of Thoracic Duct Injuries, Surgery **24**:805-810, 1948.

31. Dorsey, J. F., and Morris, G. E.: Traumatic Ruptures of the Thoracic Duct with Chylothorax, J. A. M. A. **119**:337-338 (May 23) 1942.

and plasma proteins are reduced to a small but perceptible degree.[32] Beyond 24 hours the plasma proteins fall steadily to a low of 3.8 gm. per 100 cc. in two to three weeks. It has been established for human beings, as for other mammals, that the absolute and relative amounts of chyle and its several constituents vary in a fairly direct fashion with the proportions of water, proteins, fats, and carbohydrates in the diet.

Ehrenhaft and Meyers[33] found that the blood fat levels were sharply reduced to half the normal immediately after ligation of the thoracic duct, and that a high-fat diet (150 Gm.) temporarily restored the low normal values. During the two weeks after ligation, the blood fat level gradually climbed to normal.

Sir Astley Cooper[34] found that ligation in animals with a single duct is followed, if not by immediate rupture of the receptaculum chyli, at all events by lesions which are soon fatal. He produced rupture of the receptaculum chyli by simple digital compression of the duct during digestion.

ETIOLOGY

Table 2 lists the causes of chylothorax as summarized by McNab and Scarlett[35] and by Jahsman.[28] Baldridge and Lewis[36] list the causes of traumatic chylothorax as found in the two major reviews in the literature. In Table 3 we have listed the causes of traumatic chylothorax as given by Shackelford and Fisher[3] and Lampson,[4] and we have included the additional cases that we have found in the literature. The surgical causes of chylothorax are listed in Table 4. Direct injury to the thoracic duct may occur during a surgical procedure in the neck or during an intrathoracic or upper intra-abdominal procedure (such as heart or lung surgery, esophageal surgery, rib resections, splanchnicectomies, or mediastinal procedures). Many of those injuries, with successful immediate treatment, have not been reported. Since chylothorax did not develop in these cases, they are not being discussed in this paper. Some of the causes of traumatic chylothorax are straightforward in the nature of their mechanics. These include gunshot and stab wounds, direct surgical injury, fractured ribs, and fractured or dislocated vertebrae. In Buxton and Morrison's case[7] chylothorax was prevented from developing by therapy and by the patient's vomiting the chyle from a fistula and an abscess between the thoracic duct and the esophagus. In regard to the nonpenetrating injuries, such as those with a history of falling or being thrown, an automobile accident, hyperextension of the spine, severe sneezing or coughing, convulsions, blast injuries, or birth injuries, there is some speculation about the mechanism of

32. (*a*) Whitcomb, B. B., and Scoville: Postoperative Chylothorax: Sudden Death Following Infusion of Aspirated Chyle, Arch. Surg. **45**:747-753 (Nov.) 1942. (*b*) Little, J. M.: Harrison, C., and Blalock, A.: Chylothorax and Chyloperitoneum, Surgery **11**:392-401, 1942. (*c*) Dorsey and Morris.[31]

33. Ehrenhaft, J. L., and Meyers, R.: Blood Fat Levels Following Supradiaphragmatic Ligation of the Thoracic Duct, Ann. Surg. **128**:38-45, 1948.

34. Cooper, A.: Three Instances of Obstruction of the Thoracic Duct with Some Experiments Showing the Effects of Tying That Vessel, Medical Records and Researches, London, 1798.

35. McNab, D. S., and Scarlett, E. P.: Traumatic Chylothorax, Canad. M. A. J. **27**:29-36, 1932.

36. Baldridge, R. R., and Lewis, R. V.: Traumatic Chylothorax, Ann. Surg. **128**:1056-1078, 1948.

TABLE 2.—*Etiology of Chylothorax*

A. Destructive damage to the thoracic duct or its terminals
   1. Trauma to the chest without fracture of bone
   2. Trauma to the chest with fractured ribs, clavicle, or vertebrae
   3. Accidental severance of the duct during surgery
   4. Accidental severance of one or more duct terminals during surgery
   5. Gunshot or stab wounds (relatively infrequent cause, because with such wounds an immediate fatality is more than likely from injury to one of the near-by vital structures)
   6. Perforating lymphangitis involving the duct or terminals
   7. Aneurysm of the duct with rupture

B. Obstruction to the thoracic duct
   1. Within the duct or terminals
      (*a*) new growth
      (*b*) lymphangiectasis
      (*c*) filariasis
   2. From outside the duct
      (*a*) new growth and granulomas, carcinoma, lymphosarcoma, tuberculous glands, Hodgkin's disease
      (*b*) thrombosis of the left subclavian vein
      (*c*) cirrhosis of the liver
      (*d*) erosion by aortic aneurysm
      (*e*) erosion by rubber tube, placed for empyema drainage *

C. Spontaneous or unknown origin
   Most of these lesions occur in infants, and many of them may actually have been produced by hyperextension of the spine during delivery, or they may be due to too vigorous manual attempts at resuscitation, coughing and vigorous crying, or convulsions (Pisek, G. R.: A Case of Chylothorax, Arch. Pediat. **34**:929, 1917). (The last three may change the pressure relationships of the thoracic duct.)

TABLE 3.—*Etiology of Traumatic Chylothorax*

	Shackelford and Fisher,[3] 1938	Lampson,[4] 1947	Additional
Crushing injuries	17	1	..
Wounds (bullet and stab)	8	5	2*
Fall from height	6	2	..
Blow on chest	5	2	..
Thrown against automobile seat	4	..	..
Hyperextension	1	..	..
Automobile accident with collision	..	1	..
Hit by automobile	..	1	..
Severe coughing	..	2	..
Surgical accident	..	4	3 (2†, 1, authors' case)
Convulsions	..	.	1‡
Resuscitation, vigorous	..	..	1§
Blow on abdomen	..	.	1‖
Total	41	18	8

* Whiteside and others.[50] Buxton and Morrison.[7]
† Whiteside and others.[50] Baldridge and Lewis.[38]
‡ Pisek, G. R.: Arch. Pediat. **34**:929, 1917.
§ Everhart, J. K., and Jacobs, A. A.: J. Pediat. **15**:558, 1939.
‖ Traquair, K.: Brit. J. Surg. **33**:297, 1946.

TABLE 4.—*Surgical Causes of Chylothorax and Outcome*

	No. of Cases	Result
1. Lysis of adhesions of left lung by the thoracoscope *	1	Recovery†
2. Resection of an Ewing's tumor of the right 10th rib and vertebra [39]	1	Recovery†
3. Sympathectomy [36]	1	Recovery§
4. Sympathectomy ‡	1	Death§
5. Sympathectomy [32a]	1	Death†
6. Tetralogy of Fallot operation [50]	1	Recovery§
7. Sympathectomy (authors' case)	1	Recovery†

* Douady, D.; Dupuy, O., and Bouvrain, Y.: Arch. med. chir. de l'app. respir. **13**:284, 1938.
† Conservative therapy.
‡ Peet, M. M., and Campbell, K. N.: Univ. Hosp. Bull., Ann Arbor **9**:2-3, 1933.
§ Surgical ligation.

production of chylothorax. The mechanism is thought to be stretching of the thoracic duct; because the cisterna chyli is fixed beneath the diaphragm, the right crus of the diaphragm compresses the fragile duct against the vertebrae and rupture ensues. After rupture the chyle escapes retropleurally and forms a retropleural chyloma. This has been proved by surgical exposure, x-ray examination and postmortem studies. Later the pleura ruptures, producing chylothorax. The most frequent site of rupture in nonpenetrating injuries is the subdiaphragmatic portion in the region of the ninth and tenth thoracic vertebrae. The leakage is usually into the right pleural cavity, since here the duct is on the right and does not cross over to the left until the sixth thoracic vertebra is reached. In reviewing the literature we found 65 instances of traumatic chylothorax, among which there were 37 cases of right-sided, 20 of left-sided, and 8 of bilateral chylothorax. It has been stated that the duct is more liable to rupture if the patient has just consumed a heavy meal. Cooper's work,[34] mentioned above, may lend some credence to this idea. It is felt that the intraductal pressure is greatest, and the sudden change of forces brought about by the trauma would be most destructive, at that time.

CLINICAL PICTURE

The signs and symptoms are due to the rapid accumulation of chyle in the pleural cavity. The immediate effect of the trauma is mechanical in nature, as described above. After the tear in the duct occurs the chyle collects in the mediastinum. There is some discussion as to the further course of events. Swift and Neuhof[37] describe the demonstration of "retropleural chylomas" in mediastinal tissues at operation, at postmortem examination, and on x-ray examination. Evidence in favor of retropleural chyloma formation is the fact that in Buxton and Morrison's case[7] chylothorax did not develop in spite of a tear in the thoracic duct. There were two tears in the esophagus and an abscess surrounding these. The patient continued to vomit chyle and so periodically decompressed his chyloma. If the pleura over the chyloma ruptures, chylothorax ensues, with a rapid accumulation of chyle in the pleural cavity. The time of rupture of the pleura is unsettled and undetermined. The immediate effects of the accumulation of chyle in the pleural cavity are mechanical in nature, resulting from compression of the lung, a mediastinal shift, and perhaps angulation of the great vessels. There are several other theories of the nature of the cause of the immediate effects (dyspnea and shock) of the chyle accumulation as follows: (1) anaphylactic shock[38]; (2) protein intoxication from the reabsorption of chyle[35]; (3) sudden changes in pressure relations by release into the pleural cavity.[35] Shackelford and Fisher[3] feel (on the basis of an autopsy mentioned by McNab and Scarlett) that this acute onset is due to the following chain of events: At the site of rupture of the vessel the escaped fluid becomes encysted; the encystment enlarges, causing necrosis of the adjacent pleura, and finally bursts, precipitously flooding the pleural cavity. None of these theories has been conclusively proved; Strauss[39] feels that in a bullet-wound it is the

37. Swift, E. A., and Neuhof, H.: Cervico-Mediastinal Lymphangioma with Chylothorax, J. Thoracic Surg. **15**:173-181, 1946.

38. Paitre: Traumatic Rupture of Thoracic Duct with Left Chylothorax, Bull. et mém. Soc. nat. de chir. **55**:813-816, 1929.

39. Strauss, A.: Chylothorax Due to Bullet Wound, J. Thoracic Surg. **5**:539-551, 1936.

necrosis and sudden slough of the duct wall which allows the chyle to gain access to the pleural cavity and give the sudden picture. A review of the literature reveals that the symptoms resulting from the mechanical effect of the chyle may be delayed from two days to six and a half years [40] after the injury, with the most usual time being two to 10 days. There is a sudden onset of dyspnea, accompanied with a state of shock, manifested by a rapid thready pulse, low blood pressure, pallor, cold, clammy skin, and a subnormal temperature. There is rapid and complete relief of symptoms following thoracentesis. Thoracentesis yields chyle whose characteristics are listed above. Occasionally the chyle will be masked by the presence of blood in the first few taps. Reaccumulation of fluid with the recurrence of symptoms depends on the quantitative escape of chyle into the pleural cavity.

A train of persistent secondary signs and symptoms is the result of the loss of fat, protein, fluid, and lymphocytes. These are as follows: (*a*) gradual or rapid loss of weight, (*b*) dehydration, (*c*) reduction in serum and total body protein, (*d*) disappearance of lymphocytes and eosinophiles from the circulating blood, (*e*) reduction in blood tissue fat, (*f*) inanition, oliguria, and thirst, and (*g*) death.

Traumatic chylothorax occurs in males more frequently than in females, 71% of the patients reported on having been males. This is probably related to the fact that males are more subject to injury than females. The age ranges from 15 days to 62 years.

TREATMENT

The literature abounds with prohibitions against the use of surgery ranging from Cushing's [41] statement that the duct is in forbidden territory to Florer and Ochsner's [42] statement that there is a 100% surgical mortality rate. Baldridge and Lewis [36] divide the treatment into three phases: (*a*) reduction of the volume of chyle and prevention of respiratory and circulatory collapse from the intrapleural pressure; (*b*) maintenance of nutrition; and (*c*) measures designed to favor healing of the injured duct.

(*a*) Reduction of the volume of chyle and the prevention of collapse are accomplished by the limitation of fluid intake, use of a low-fat diet, avoidance of lymphagogues, especially intravenous administration of fluids, and repeated thoracenteses.

(*b*) Maintenance of nutrition consists in administration of a high carbohydrate, high-protein, low-fat, high-vitamin diet; maintenance of fluid balance; transfusions of blood, plasma, and blood substitutes; feeding of chyle by mouth; feeding of chyle by rectum (based on the fact that the lymphatic drainage of the rectum is into the superficial system and circumvents the thoracic duct [43]); intravenous, intrasternal, and intramuscular [44b] administration of chyle, and intravenous administration of

40. Beatty, O. A.: Chylothorax; Case Report, J. Thoracic Surg. **6**:221, 1936.

41. Cushing, H.: Wounds of the Thoracic Duct, Ann. Surg. **27**:719, 1898.

42. Florer, R., and Ochsner, A.: Traumatic Chylothorax, Surgery **17**:622-629, 1945.

43. Hall, E. H., and Morgan: A Case of Chylous Ascites, Quart. Bull. Northwestern Univ. M. School **2**:44, 1900.

44. (*a*) Bauersfeld, E. H.: Traumatic Chylothorax from Ruptured Thoracic Duct Treated by Intravenous Injection of Aspirated Chyle, J. A. M. A. **109**:16-18 (May 22) 1937. (*b*) Oeken; Ein Fall von Zerreissung des Ductus thoracicus infolge Brustquetschung, München. med. Wchnschr. **55**:1182-1183, 1908. (*c*) Smith and Woliver.[29]

45. Holt, L. E.; Tidwell, H. C., and Scott, T. F. McN.: Intravenous Administration of Fat, J. Pediat. **6**:151, 1935.

emulsified fats.[45] Schnug and Ransohoff [46] suggest doing a skin test before parenteral administration of chyle in an effort to avoid anaphylactic reactions.

(*c*) Measures designed to favor healing of the injured duct include phrenicotomy [25] (the mechanism of action of a phrenicotomy is due presumably to elongation and narrowing of the crural sulcus, with apposition of the diaphragmatic and mediastinal parietal pleuras. Other mechanisms such as the elimination or diminution of the aspirating action of the respiratory movements on the open thoracic duct must also operate. Nowak and Barton [25] suggest also that it is possible that the limitation of the respiratory movements favors clot formation of lymph by eliminating the defibrinating action ascribed to these movements in the case of hemothorax); phrenic neurotripsy, phrenicolysis, or pneumoperitoneum to elevate the diaphragm and cause compression of the mediastinal tissues; pneumothorax [31] to lessen the flow; retropleural drainage,[6] with the thought that a free external flow of inspissated chyle would encourage healing of the rupture in the duct and that spontaneous closure of the mediastinal sinus will occur, thus preventing rupture or diffusion into the pleural space; thoracotomy, done to eliminate the suction of the negative pressure (to be avoided because of the danger of the development of empyema); thoracoplasty; intrapleural injections of sterile broth,[47] gomenol in oil (cajuput oil),[48] and chloroazodin ("azochloramid") to stimulate a fibrinous reaction; roentgen-ray treatment (especially if rupture of the duct is due to a neoplasm) to stimulate the shrinkage and fibrosis; and surgical ligation (not advised early because a traumatized thoracic duct will often close or heal spontaneously). If an injury to the duct occurs during an operation and it is recognized, there are several methods of treatment possible: (*a*) suture of a tear,[41] with or without plication of overlying tissues; (*b*) ligation of the severed ends of the duct (and all visible, divided lymphatic vessels) and/or application of thrombin-soaked gelfoam® [49] (or a comparable agent) or of a piece of muscle [32]; (*c*) injection of sodium morrhuate into the tissues to produce fibrosis [50]; (*d*) implantation of the severed duct into a near-by vein,[51] and (*e*) tamponade. Ligation of the thoracic duct in the lower third is not considered safe because the collateral circulation is not as rich as in the upper third and rupture from high intraductal pressure is brought on by an acute obstruction.

As stated above, surgical exploration is not advised early because a traumatized thoracic duct will often close or heal spontaneously. Surgical intervention and ligation of the thoracic duct for the treatment of chylothorax has been reported infrequently until recently. Exploration through the chest is justified if conservative measures fail and it is clear that spontaneous closure is unlikely. In attempting to locate the duct, it is suggested by Shackelford and Fisher [3] that the patient be

46. Schnug, E., and Ransohoff, J.: Traumatic Chylothorax, Surgery **14**:278-281, 1943.

47. Rienhoff, W. F. Jr.: Pneumonectomy, Bull. Johns Hopkins Hosp. **53**:390-393, 1933. Schnug and Ransohoff.[46]

48. Matson, R. C., and Stacy, J. W.: Traumatic Chylothorax, Dis. Chest **6**:332-336, 1940.

49. Smithwick, cited by Baldridge and Lewis.[36]

50. Whiteside, W. C.; Stewart, W. D., and Cuthbertson, A. N.: Traumatic Chylothorax, Canad. M. A. J. **61**:374-376, 1949.

51. Deansly, E.: A Case of Implantation of the Divided Thoracic Duct into the Internal Jugular Vein: Recovery, Lancet **2**:1783, 1903. Harrison, E. On the Treatment of Wounds of the Thoracic Duct, Brit. J. Surg. **4**:304, 1916. Hodge and Bridges.[30]

given a pint (500 cc.) of cream to which has been added either Scharlach R or Sudan III about one and a half hours before operation. After exposure of the duct, any of the above procedures or combinations thereof may be carried out.

PROGNOSIS

The literature gives a mortality rate of approximately 50% for the condition traumatic chylothorax [52] in spite of the type of treatment. In our review of the total literature we have found 66 acceptable cases (including our own), with recovery in 39 cases and death in 27 cases, a mortality rate of 40.9%. Table 5 is an attempt to break down this figure into its component parts. The small number of cases in the surgically treated group precludes any definite conclusions. However, the recent reports of Whiteside,[50] Lampson,[4] and Meade [53] offer some promise.

In our own case, conservative therapy was decided on because of the patient's continued excellent physical status.

TABLE 5.—*Analysis of Treatment*

	Conservative Measures		
	Died	Recovered	Total
	20	28*	48
	Surgical Measures		
	Died	Recovered	Total
Thoracotomy with rib resection	4	4	8
Mediastinotomy	1	..	1
Tamponade, cervical duct	..	1	1
Ligation, cervical duct	..	1	1
Phrenic neurotripsy	1	2†	3
Thoracotomy with ligation	1	4‡	5
Total	7	12	19

* Includes authors' case.
† In one patient a rent in the cisterna chyli was sutured afterward, and one patient was given sterile broth injections.
‡ One patient underwent phrenic neurotripsy.

REPORT OF A CASE

J. M. was a 40-year-old white woman admitted to the Sinai Hospital on Sept. 15, 1948, and discharged on November 16. This patient was admitted with a three-year history of frontal headaches and known hypertension. Six months before her admission she noted palpitation, precordial pain, exertional dyspnea and occasional ankle edema. A complete medical and hypertensive evaluation showed her to be an excellent candidate for a thoracolumbar sympathectomy. On September 22, a right thoracolumbar sympathectomy and splanchnicectomy (Hinton and Lord) [54] were performed without any operative difficulty (pleura was not entered). Postoperatively the patient's blood pressure ranged from 140 to 160 mm. systolic and from 100 to 110 mm. diastolic. From the second postoperative day on, she showed suppression of breath sounds and impaired percussion note over the entire right base, but with no respiratory difficulty. On the 15th postoperative day she began to show exertional dyspnea. A roentgenogram of the chest showed right pleural effusion. Thoracentesis on October 16 yielded 1,125 cc. of fluid, the characteristics of which will be described below. The patient's only complaint during the ensuing five months was exertional dyspnea, relieved by thoracentesis. Over the period of

52. Shackelford and Fisher.[3] Jahsman.[28] Baldridge and Lewis.[36] Lampson.[4]

53. Meade, R. H.: Personal communication to Lampson.[4] Crafoord, C.: A Contribution to Thoracic Duct Surgery, Acta. chir. scandinav. **85**:99-113, 1941.

54. Hinton, J. W., and Lord, J. W., Jr.: Operative Technique of Thoraco-Lumbar Sympathectomy, Surg., Gynec. & Obst. **83**:643-646, 1946.

the next five months she had 10 thoracenteses, yielding a total of 11,405 cc. of fluid. The final tap was done while the patient was still on the operating room table, after the left thoracolumbar sympathectomy and splanchnicectomy on Feb. 11, 1949. The postoperative course was uneventful, and roentgenograms of the chest were clear of effusion. The patient was last seen by one of us (E. H.) on Nov. 27, 1949, at which time she was completely relieved of headaches, had no exertional dyspnea, palpitation or precordial pain, a blood pressure of 148/96 (right) and 154/94 (left), and a normal chest roentgenogram.

The fluid obtained on each thoracentesis was examined and found to have the following characteristics: (1) café au lait color, (2) specific gravity of 1.020, (3) sterile cultures, (4) presence of fat globules which took Sudan III stain, (5) a yellow ether extract layer, and (6) an occasional red cell on microscopic examination. The peripheral blood picture was carefully followed. There was never any significant variation in the lymphocytic distribution until Nov. 2, 1948, at which time there was a drop in the percentage of lymphocytes from 22 to 16%, with a persistence at this level. The total white blood cell count ranged between 6,100 and 8,600. There was always 2 to 4% eosinophilia.

The treatment of this patient's chylothorax was conservative in nature. This course was chosen because the patient always maintained her excellent physical status and complained only of moderately severe exertional dyspnea, relieved by thoracentesis. The conservative course consisted of limitation of fluids given intravenously, administration of a low-fat diet and supplemental vitamins and repeated thoracenteses.

SUMMARY

The embryology, anatomy, and physiology of the thoracic duct have been reviewed. The etiology, clinical picture, treatment, and prognosis of traumatic chylothorax have been reviewed, and a report of the second successfully treated, reported case of chylothorax following a thoracodorsal sympathectomy is presented. A tabulated summary of every previously reported case of traumatic chylothorax is given.

ADDENDUM

Since submission of this article for publication, we have encountered 10 other cases of traumatic chylothorax recorded in the literature. Two were reported by Shumacker and Moore [55] following tetralogy of Fallot operations, and the patients were successfully treated by surgical ligation of the thoracic duct. One case (Douady and others [56]) followed a pneumonolysis, and the patient recovered with conservative therapy. Meade and others [57] report successful treatment in two cases following injury, in one by ligation of the thoracic duct and in one by closed drainage of the pleural cavity. In discussing Meade's paper, Rumel, Klepser, and Touroff describe a total of four cases secondary to injury, stab, and bullet wounds, all with recovery. Two of the patients were given conservative treatment, including intravenous administration of chyle; the other two were treated by surgical ligation of the thoracic duct. Lowman and others [58] report a case secondary to trauma in which conservative treatment was given, with recovery.

These additions will change slightly the figures in Tables 2, 3, and 4 and give a more favorable outlook for surgical ligation of the thoracic duct.

55. Shumacker, H. B., Jr., and Moore, T. C.: Surgical Management of Traumatic Chylothorax, Surg., Gynec. & Obst. **93**:46-50, 1951.

56. Douady, D.; Dupuy, D., and Bouvrain, Y.: Chylothorax benin apres section d'adherences pleurales, Arch. med. chir. de l'opp. respir. **13**:284-291, 1938.

57. Meade, R. H., Jr.; Head, J. R., and Moen, C. W.: The Management of Chylothorax, J. Thoracic Surg. **19**:709-723, 1950.

58. Lowman, R. M.; Hoogerhyde, J.; Waters, L. L., and Grant, C.: Traumatic Chylothorax, Am. J. Roentgenol. **65**:529-546, 1951.

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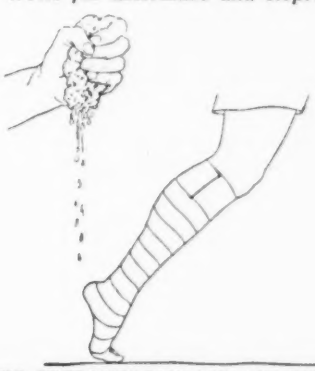

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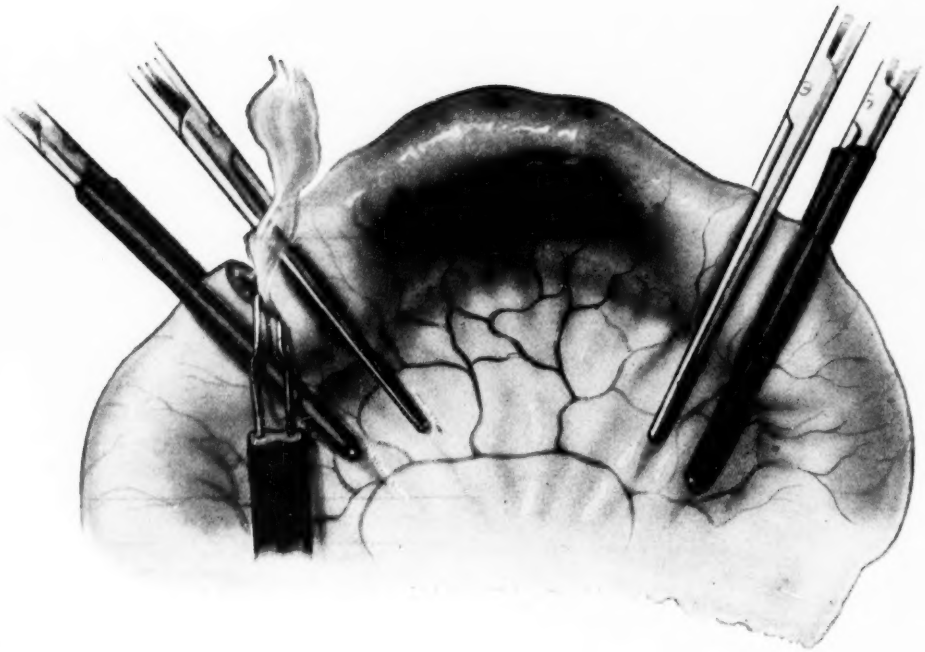

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DiCaprio, J. M., and Rantz, L. A.: Arch. Int. Med. 86:649 (Nov.) 1950.

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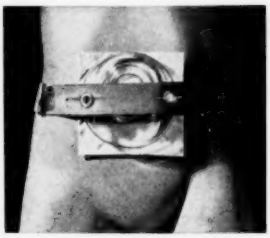

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